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THE AMERICAN JOURNAL OF PHARMACY

VOL. 94.

OCTOBER, 1922.

No. 10.

EDITORIAL

THE MASTER FORMULA—HONOR, INTEGRITY AND TRUSTWORTHINESS.

Professor Remington delighted in relating to his classes anecdotes concerning his experiences in the Squibb Laboratories, and his close acquaintance with the venerable Dr. Squibb gave him unusual opportunities to appreciate and record that great man's love of truth and honest practice. A reminder of one of Professor Remington's characteristic and inspirational talks came to us recently while reading a booklet issued by the House that Squibb Built. The little paragraph ran something like this:

During the Civil War a certain material used in making one of the Squibb products became very scarce and its price extremely high. One of the young chemists employed in the laboratory suggested to Dr. Squibb that another ingredient be substituted—one which cost less and was easier to obtain, but was not quite so satisfactory. "By changing your formula in this way," the young man argued, "you will save money and most people will never know the difference."

"Young man," said Dr. Squibb, "I am always willing to change a formula when I can improve it. But please remember that—THE MASTER FORMULA OF EVERY WORTHY BUSINESS IS HONOR, INTEGRITY AND TRUSTWORTHINESS. THAT IS ONE FORMULA I CANNOT CHANGE."

Dr. Squibb had sensed aright the message of the unchanging formula. For it was according to its prescription that he compounded the great business concern bearing the mark of Squibb, which long after the passing away of its sponsor continues to draw sustenance and luster out of every letter of his illustrious name. He knew well the inalterableness of the Master Formula—knew well that not even

Time, that insufferable changer of all things material—could ever substitute another for any of the priceless ingredients in this Master Formula, the universal code of ethics.

At random intervals in History, and out of queer, scattered corners of the earth, exponents of the Master Formula have come to Man to describe and prescribe its priceless ingredients. Confucius, of Shantung, the Sage of China; Buddha the Silent, the god of Dark India; Mohammed, Lord of Islam, Soldier and Saviour (?) too; and Jesus of Nazareth, Prince of God, who taught that the Master Formula was the Master's Formula too. All have told the same old story—the story of this recipe for human happiness. The Master Formula indeed has had many great interpreters, and the world would be a better place to live in if its people could properly grasp their interpretations.

And oh! for a keener appreciation today—this today of so much insincere dealing, this today of unfinished tasks, this today of questionable business practices. Oh, for a real understanding of the infallibility of this prescription; of the certainty of the finished product,—this Master Formula—conceived in the depths of Ago and destined to proclaim the obligations of man to his kind as long as the Universe rolls on within its steady system.

HONOR, INTEGRITY and TRUSTWORTHINESS, they are the Priceless Ingredients. And no one can deny the harmony of these constituents—they are compatible to every extreme and out of their ultimate fusion in the crucible of life inevitably comes the crystal clear solution, the quintessence of human desires—the true God-given Happiness.

I. G.

THE ROMANCE OF PHOSPHORUS.

Tax Collector Bauduin had much spare time on his hands, for the thrifty citizens of the little community of Grossenhayn, in Saxony, paid their tax bills promptly and thereby avoided a penalty. Much of this spare time was spent in earnest gossip in the shoe-mending shop of one Freuben, an eccentric cobbler who had a local reputation as a dabbler in the dark art of alchemy.

One can surmise, then, of the visionary schemes which this peculiar pair indulged in. These were the days when the search for the Quintessence used up the Alchemists' time and efforts. Four

elements they already had, namely earth, fire, water and air, and the fifth—the quintessence, still remained. Freuben, over his last, discussed with the idling Bauduin the possibility of obtaining this fifth essence by combining together the four known essences in an alembic, and then distilling. Thus they conceived that they could obtain the spirit of the world (*spiritus mundi*).

Calx they dissolved in spirit of nitre, the resulting solution they evaporated to dryness, and the residue exposed to air so that it might absorb "humidity." A second distillation was resorted to, and thus was obtained in pure form the long-sought-for quintessence—the virile, potent "humidity."

To prove that "seasons change but human passions never," they placed on sale as a panacea for all human ills, their "captured humidity" at a price of 12 *groschen* per *loth* (approximately sixty cents per ounce) and afflicted rich man and beggar man eagerly came to buy. The alchemists became rich—they had indeed found the philosopher's stone—the *spiritus mundi*.

Freuben threw away his last and purchased a decadent villa and spent his *spiritus mundi* in its reconstruction. Bauduin did not come up for re-election for the first time in many years, and a new tax collector was duly installed in office. Instead he cultivated music and also continued experimenting. One night during the course of his experiments Bauduin dropped and broke a cumbersome lambik containing some of the calcined nitrate of lime, and was surprised to find it luminous in the dark. He also observed that this luminosity came after exposure of this material to sunlight. He promptly recognized the importance of his discovery, and taking some of the "inspired earth" to Dresden City he found Kunckel, a royal pharmacist of that city very eager and anxious to learn all about the queer substance.

The ethics of those days seemed to be almost as flexible as they are today, for history tells us that Kunckel promptly visited with Bauduin so that he might extract from the "ignorant dabbler" the formula for his essence. But Bauduin was wary, and when the visitor spoke of essences and retorts, Bauduin extravagantly discussed cadences and rhapsodies. Finally under some pretext or another, Kunckel induced the alchemist to leave the room for a few minutes, and during this interval the royal pharmacist managed to purloin a fragment of the precious "inspired earth" by nipping it with his finger nail.

Thus it was that Kunckel managed to get material and information with the aid of which he worked out a process of preparing the luminous earth, which Bauduin very discreetly had called Phosphor. Incidentally it is told that when he eventually did produce some of this material, he courteously sent a little morsel of it to Herr Bauduin as a slight memento of the instructive and interesting musical evening that the alchemist had given him.

Later the ethical Kunckel found that another alchemist had "gone one better," and had produced not "inspired earth" but the very "inspiration" itself—the real *phosphor*. Brandt, of Hamburg, an old physician-alchemist, had indeed produced from human urine the element itself, and Kunckel anxiously sought to obtain an interview with the old gentleman, probably expecting to repeat his light-fingered experiment. However he confided the news to a friend bearing the fitting name of Kraft, and the latter immediately justified his name by taking a special post to Hamburg and purchasing outright from Brandt, the secret art and mystery of preparing phosphorus. This he did clandestinely and Kunckel was hoist with his own petard.

However, it is told that Kunckel later on managed to inveigle Brandt, through an intermediary named Homberg, to furnish him also with the precious formula. In payment whereof he furnished Brandt with a curious little device, then quite novel, consisting of a vari-colored little house tenanted in turn by a wooden man and a wooden lady—the former, as usual, staying indoors when the weather was stormy, and emerging when the sun was in smiles, one of those toy weather forecasters that are quite as reliable as the more modern and elaborate Government establishments that have the same purpose of existence.

And thus it was that Kunckel after all became possessor of the secret and soon established himself as the first practical manufacturer of phosphorus.

This is the story of the discovery of phosphorus, replete with oddities and incongruities—but it is interesting despite the fact that it rather disillusionizes the believer in the chivalry and honor of other days. Surely the world is getting better if written codes of ethics be any criterion.

I. G.

(With acknowledgment to *Wootton's Chronicles of Pharmacy*.)

SELECTED EDITORIAL

NEW LIGHT ON THE ORIGIN OF LIFE.

By Dr. Edwin E. Slosson.
(Science Service)

Was the first living being a plant or animal? How could either originate out of non-existing matter?

These are questions that have hitherto baffled scientists. They could trace back, more or less satisfactorily, the lines of development of plants and animals to the simplest and most primitive forms of life, but there they ran up against an insurmountable wall on the near side of which was the world of living organisms and on the far side the world of inert mineral and inorganic matter.

We all know that non-living matter can be converted over into living matter for we do that ourselves whenever we eat or breathe. We all know that green plants have the power of building up sugar and starch and wood (the so-called carbohydrates) out of the water of the soil and carbon dioxide of the air, for we can see them do it any sunny day. But it is life only that can bring into the living organism this inorganic material. Water and carbon dioxide, which is plain "soda water," does not spontaneously change over into sugar or start to grow into a plant. It requires green colored granules of the leaves, called chlorophyll, to effect this transformation.

But chlorophyll is a very complicated chemical compound. It is formed only by green plants as they develop in the sun's rays from white sprouts. So the plant must exist before chlorophyll is formed. But on the other hand a plant could not exist unless it got its energy from the sugar and other stuff stored up previously by some chlorophyll-bearing plant. Even the simplest green plant cannot live and grow on its nutritive salts in the sunshine unless it has a bit of plant-stuff to feed on as a starter.

We might surmise as a way out of the dilemma that animal life came first on the earth and in decaying supplied the primitive plants with the necessary organic food stuff. But here we are blocked be-

cause animals are parasites of plants. They live on the sugars and so forth that the green leaves have stored up by means of sunshine.

So this was the perplexing situation. Plants can feed on animals or other plants. Animals can feed on plants or other animals. But where could the first animals or plants get food when there was nothing but mineral matter in the world? It was worse than the old question, which came first, the hen or the egg?

But of late we are beginning to get light on the problem. The wall between the living and non-living is crumbling down. Certain sugars and proteins, such as the plant forms that we eat, can now be made in the laboratory out of inorganic material. Artificial cells have been constructed that grow and crawl and feed themselves and stick out feelers and sub-divide very much like living cells. It has been found that ultra-violet rays, that is, light of such short waves that it cannot be seen, can convert water and carbon dioxide into sugar as chlorophyll does.

These short waves are not contained in the sunshine that reaches the earth today, but it is found that ordinary rays may act the same way in the presence of certain substances such as iron rust in water. These same energetic rays are able to incorporate the nitrogen of mineral salts into compounds like the protein of the living cell. So here we see the possibility that the action of the sunlight on the sea in primordial periods—or even in the present—might produce sufficient food to give a single cell a start in life and enable it to grow and multiply and develop into other and higher forms.

But how this primal cell got to going in this way the biologists are only beginning to surmise. Dr. E. J. Allen, at the recent Hull meeting of the British Association for the Advancement of Science, ventures the theory that the first organism was of the animal sort and spherical shape, but that it gradually grew a tail or whip that enabled it to rise to the sunny surface of the sea whenever it sank below and that it there acquired the chlorophyll by which it could make its own food out of the air and water. This is far from knowing what did happen in those early days, but it is a great advance to be able even to speculate as to how it might have happened since not many years ago it seemed that it could not happen at all.

ORIGINAL PAPERS

THE TOXIC CONSTITUENT OF GREASEWOOD (*SARCOBATUS VERMICULATUS*).*

By James F. Couch.

Introduction. *Sarcobatus vermiculatus*, known in the mountain States as "greasewood," is a perennial, classified in the Chenopodiaceae. It occurs abundantly on "alkali" soils in the semi-arid valleys, is somewhat bushy, and generally grows to a height of four to five feet. The stems and larger branches are tough and woody; the green succulent portions of the plant are the leaves, blossoms, fruits and the very small, recently grown branches. All of these latter are salty and alkaline to the taste without perceptible acidity. This lack of acidity is of considerable interest in connection with the problem of the manner in which the plant acids are combined.

Although greasewood is an important fodder plant and is extensively grazed by sheep upon the winter range, it has caused several well-authenticated cases of poisoning in these animals. In order to establish the facts connected with the poisonous properties of the plant a detailed study of the subject was begun by the Office of Investigations of Stock Poisoning by Plants, of this Bureau. The preliminary results of this investigation are in course of publication by the Bureau of Animal Industry.

The writer was assigned the task of determining the nature of the poisonous principle, and an account of the chemical study of the plant forms the subject matter of this communication.

The problem was first proposed and the investigation was begun while the writer was engaged in field work at the experiment station near Salina, Utah, maintained by the Bureau of Animal Industry for the study of stock-poisoning plants. A number of extracts of the fresh plant were made; these were administered to sheep either without further treatment or after fractionation to include or eliminate certain classes of substances. Of 12 sheep used in these experiments, two were made sick and two others were killed by the extracts administered. As a result of this work it was definitely known that the poisonous constituent is soluble in water, insoluble in alcohol; and the common organic solvents, is not alkaloidal,

*Contribution from the Pathological Division, Bureau of Animal Industry, United States Department of Agriculture, Washington, D. C.

glucosidal, nor saponinic, but is a mixture of neutral potassium oxalate and neutral sodium oxalate. The proportion of oxalic acid (deprived of the potassium) in the plant is not great enough to cause symptoms of poisoning in sheep in doses thrice that of the lethal dose of plant when force-fed (as determined by Marsh, Clawson and Couch), and the proportion of potassium itself (deprived of oxalic acid) is likewise not great enough to cause poisoning in the same large doses. This consideration led to the conclusion that the poisoning is due to the salt, potassium oxalate, mixed with sodium oxalate, and this mixture is, therefore, stated to be the toxic constituent.

Earlier Investigations of Sarcobatus. The greasewood early attracted attention because of its alkali-resisting properties and its fodder value. It was, therefore, subjected to analysis in several institutions. One of the earliest of the published reports was by Goss and Griffin,¹ who made an extensive study of the soil conditions in the Rio Grande and Animas valleys of New Mexico. Their analysis of the ash of the air-dried plant showed:

	Per cent.
Ash	13.12
Silica	3.00
Potash	22.06
Soda	23.89
Lime	6.52
Magnesia	1.35
Manganese	Trace
Fe and Al, by difference	4.73
P ₂ O ₅	4.12
SO ₃	4.33
Carbon dioxide	23.80
Chlorine	8.01
<hr/>	
Total	101.81
Oxygen equivalent of chlorine	1.81
<hr/>	
Corr. total	100.00

These results show the large proportion of potassium and sodium in the plant, and the amount of carbon dioxide points to a large proportion of organic acid.

The ash of *Sarcobatus vermiculatus* was investigated by the

¹ *New Mexico Sta. Bul. No. 22*, March, 1897. "Alkali in the Rio Grande and Animas Valleys." By Arthur Goss and H. H. Griffin.

Division (now Bureau) of Soils of the Department of Agriculture. The plant specimens which were used were collected near Salt Lake, Utah, about 150 miles north of the region where the plants studied by the writer were collected. The results of the study in the Division of soils were reported in two papers, the first by Cameron and Gardner,² who state: "A striking feature was the much greater percentage of ash obtained from the leaves and blossoms than from the stems, and the markedly larger percentage of alkali salts in the ash of the former. Another interesting point is that the leachings of the air-dried leaves and blossoms were shown to contain about three times as much sodium as would be necessary to balance the hydrochloric and sulfuric acids in the plant. It is, therefore, probably present very largely in organic combination and upon the decay of the plant tissues would be expected to yield large amounts of sodium carbonate."

A second publication from the Division of Soils³ contains the following data:

	Leaves and Blossoms.		Stems.
	I.	II.	
Ash % of Plant	25.85	23.47	4.94
Sodium Carbonate, % of Ash	51.93	57.90	29.46
Sodium Chloride, % of Ash	20.47	22.24	14.31
Sodium Sulfate, % of Ash	7.97	—	3.69

Two 5-gm. samples of the leaves and blossoms extracted with water gave a slightly acid extract which contained 5.81 per cent. and 5.68 per cent. of sodium chloride. Two samples of leaves and blossoms, subjected to the Carius process, yielded silver chloride equivalent to 5.43 per cent. and 5.43 per cent. of sodium chloride.

Forbes and Skinner⁴ reported a proximate analysis of *Sarcobatus* as follows:

	Per cent.
Water	4.55
Ash	14.41
Protein	19.86
Fiber	24.50
N free extract	34.28
Ether extract	2.45

² *Proc. Soc. Prom. Agric. Sci.*, 1900; pp. 162-3. "Formation of Sodium Carbonate or Black Alkali by Plants."

³ "Formation of Sodium Carbonate or Black Alkali by Plants." By Frank K. Cameron, in *Report No. 71, U. S. Dept. Agric.*, 1922; pp. 61-70.

⁴ *Fourteenth Annual Report, Arizona Exp. Sta.*, 1903; p. 349.

In Bulletin No. 94 of the California Station, E. W. Hilgard⁵ reports an analysis of the ash of "*Sarcobatus vermiculatus*" made by M. E. Jaffa. The plant used was collected in Kern County, California, and was later found to be *Allenrolfea occidentalis*⁶ and not *Sarcobatus*.

None of the earlier investigators determined the nature of the organic acid with which so much of the basic elements of the plant is combined.

The Present Investigation.

The Material. The material used in the present investigation was all collected at the same place, *viz.*, the sandy valley at the mouth of Salina Canyon, about one and one-half miles east of the city of Salina, Utah. The elevation at this place is about 5,100 feet above sea level. The collections were made at intervals during the months of July, August and September, 1921, and included plants in flower and in fruit. The greater part of the material was used immediately after collection; the remainder was air-dried under cover. The whole was carefully hand-picked and the larger woody and inedible stems were discarded. The material used for chemical examination was identical in all respects with that fed to the experimental sheep by Marsh, Clawson and Couch. The portions of the extracts which remained after the animal experiments were concluded, together with a quantity of the air-dried plant, were shipped to Washington, D. C., in September, 1921, and the investigation was continued at that place.

Methods. The determination of the ash, oxalic acid content, and water-soluble material in *Sarcobatus* present certain difficulties, and it was necessary to devise some modifications of ordinary analytical procedure in order to obtain true results. In the ashing of the plant the large amounts both of carbonates and of chlorides cause much trouble, the first by fusing and enveloping particles of carbon, which cannot then be oxidized, and the second by their volatility, which prevents the use of high temperature. It was finally found possible to ash the plant properly and to obtain concordant results by

⁵ "The Fertilizing Value of Greasewood." *Calif. Sta. Bul. No. 94*, 1891.

⁶ Cf. *Calif. Sta. Bul. No. 125* (1899), p. 28, and *Bul. No. 128* (1899), p. 38. This plant is known as "greasewood" in Southern California.

proceeding as follows: The weighed sample, preferably in a platinum dish or crucible, is dried to constant weight in an electric oven at 110° ; then the covered crucible containing the dry sample is heated on an asbestos board over a Bunsen flame at a low temperature until the greater part of the volatile organic products has been driven off, the greatest care being taken that the temperature is kept so low that the alkaline carbonates do not fuse. By proceeding in this way there is obtained a friable mass which contains the ash mixed with some carbon. To eliminate the latter the open crucible is heated over a free, hot flame in such a way that the temperature reaches dull redness in about half a minute and, as soon as the carbonates begin and weighed. The ash thus obtained is slightly gray in color, but in to fuse, the heat is removed and the crucible is cooled in a desiccator no case was the carbon content weighable.

The oxalic acid was determined by precipitation with calcium chloride under the usual analytical conditions and weighing the calcium oxide remaining from the ignited precipitate. The large amount of colloidal matter in the plant extract caused considerable trouble by preventing the proper deposition of the precipitate and making it impossible to accomplish a complete separation by filtration. These difficulties were overcome by proceeding in the following manner: Weighed portions of the plant were extracted with boiling water in successive portions until no further test for the acid could be obtained in the last portion. The filtered and mixed aqueous solutions were made slightly alkaline with ammonium hydroxide and were then evaporated just to dryness. The extract was kept in a warm place for at least 24 hours and was then redissolved in warm, distilled water, filtered, if necessary, from flocculated protein, made alkaline with ammonium hydroxide, acidified with acetic acid, heated to boiling, and precipitated by a hot solution of calcium chloride with vigorous stirring, kept hot for six to seven hours, allowed to cool over night, filtered through an ashless filter paper, thoroughly washed and the precipitate ignited over a Meker burner until the weight of the residue was constant. From this the amount of water-soluble oxalic acid was calculated.

The marc from the water extraction was then extracted with hot hydrochloric acid in order to determine the quantity of calcium oxalate in the plant. The filtered extract was made alkaline with ammonium hydroxide, which precipitated the calcium oxalate, and,

to avoid difficulties in filtration, the whole was evaporated just to dryness, allowed to stand, redissolved in hot 1 per cent. hydrochloric acid, treated with ammonium hydroxide, and then with excess of acetic acid, and the calcium oxalate was filtered off, washed, ignited, and weighed as calcium oxide.

By this procedure concordant results could be obtained, especially with the determination of the calcium oxalate. The results obtained are recorded in Table I. Two different samples of the plant were used. No. 21-160 was collected August 25, 1921, and No. 21-168 was collected September 13, 1921. The latter sample had all been ground to a coarse powder so that it was impossible to separate the fragments of the stems from the leaves. No. 21-160 was therefore used as a source of the leaves and stems analyzed.

TABLE I—OXALIC ACID CONTENT OF DRIED PLANT.

	Leaves, Stems, Fruit.	Stems.	Leaves.
	No. 21-168. Per Cent.	No. 21-160. Per Cent.	No. 21-160. Per Cent.
Moisture	8.64	5.82	5.50
Ash, as of Dry Plant	12.25	10.11	24.79
Water Soluble Oxalic Acid, Anhy- drous	9.40	2.35	10.47
Calcium Oxalate, $\text{CaC}_2\text{O}_4 \cdot \text{H}_2\text{O}$...	3.47	4.95	2.80
Total Anhydrous Oxalic Acid	11.54	4.37	12.20

Experimental.

1. *The Isolation and Identification of Oxalic Acid.* Five kilos of the fresh plant, leaves, stems and fruits were passed through a meat chopper and the minced product was packed into a tinned iron percolator and completely extracted with hot water. The watery extract when heated developed the characteristic odor of canned tomatoes. It was concentrated by evaporation to a small bulk, a sample was taken for tests, and the remainder was reduced to the consistency of a soft extract. The sample taken for tests gave the following reactions: silver chloride threw down a heavy, curdy precipitate insoluble in nitric acid and soluble in ammonium hydroxide; barium chloride produced a heavy white precipitate, almost completely soluble in dilute hydrochloric acid but insoluble in acetic acid; ammonium oxalate produced no precipitate; hydrochloric acid caused no change in the cold, but on warming, an acrid gas, resembling furfural, was

evolved; the extract was slightly acid to litmus; it did not reduce alkaline copper solutions, but after heating with mineral acids and alkalizing it caused a copious precipitation of cuprous oxide. On heating the solution with sodium hydroxide an alkaline gas with a faint odor of trimethylamine was evolved; when acidified with hydrochloric acid the solution gave a faint precipitate with Mayer's reagent, but no alkaloid could be removed by shaking the alkaline solution with immiscible solvents; on mixing the solution with a saturated solution of tartaric acid and allowing to stand, a heavy precipitate of potassium acid tartrate crystallized out.

A solution of a part of the extract was made so that 1 ml. was the equivalent of 1 gm. of green plant. The ash, extract, and oxalic acid content of this solution was determined, *viz.*,

10 ml. yielded:

Anhydrous oxalic acid, 0.2258 gm. or 2.26% of green plant.

Extract, total solids, 1.0933 gm. or 10.933 gm. per 100 ml.

Ash, 0.4720 gm. or 4.72% of green plant.

The main portion of the solution, equal to 900 gm. of green plant, was concentrated to about one-half its volume, slightly acidified with hydrochloric acid and kept in a cold place. After two weeks some twenty grams of crystals mixed with much amorphous matter had been deposited. The solution was decanted from the solid matter and this was subjected to repeated recrystallization until a pure, white, crystalline product was obtained. A solution of this substance in water was positive to the usual tests for oxalates and to Chernoff's⁷ very beautiful color reaction for oxalic acid. Analysis of the bases showed 41.24 per cent. of the total bases potassium, and the remainder (or 58.76 per cent.) sodium. Another portion of the substance was mixed with alcohol and an excess of con. hydrochloric acid was added. The mixture was warmed and stirred and after an hour was filtered. On removing the alcohol a white crystalline substance remained which responded to tests for oxalic acid. The substance was, therefore, a mixture of sodium and potassium acid oxalates.

⁷ J. Am. Chem. Soc., 42, 1784 (1920).

2. The Evidence of the Toxicity of the Oxalates in the Plant.

An aqueous extract of 10 kilos of the green plant similar to that described under one was concentrated to a small volume and was then repeatedly extracted with large volumes of hot alcohol. By this means the extract was divided into two fractions, an alcoholic solution and an insoluble residue. The substances dissolved by the alcohol were recovered by removing the solvent and a portion equivalent to 2,000 gm. of the green plant (about thrice the M. L. D.) was dissolved in a little water and was administered per os to sheep No. 622 without affecting the animal. The alcohol insoluble residue weighed 480 gm. and consisted of the mixed oxalates of sodium and potassium with small amounts of proteins, gums, and carbohydrates. Analysis subsequently showed it to contain 39.78 per cent. of anhydrous oxalic acid. Ninety-six grams of it, equivalent to 2,000 gm. of green plant, were dissolved in a little water, filtered from some insoluble matter, and were administered per os to sheep No. 638. The animal became sick, the symptoms being rapid and shallow respiration, weak and rapid pulse, and increased temperature. It finally died in cardiac collapse 2 hours and 57 minutes after the dose was administered. The symptoms shown were not different from those observed in animals poisoned by feeding on the plant.

The Oxalic Acid Alone.

Another portion of this alcohol-insoluble mass, of the same weight, *viz.*, 96 gm., equivalent to 2,000 gm. of green plant, was dissolved in water, filtered, and the greater part of the potassium was removed from the solution by precipitation as the acid tartrate, leaving all the oxalic acid in solution. The solution was then administered per os to sheep No. 631, without affecting the animal. This shows that the oxalic acid, *per se*, is not in sufficient concentration to account for the range poisoning.

The Potassium Alone.

In order to determine what rôle the potassium may play the following experiment was performed: Fifteen hundred grams of the green plant was charred over a moderate flame until all the organic matter was destroyed and only the ash with a large amount of carbon remained. The soluble materials were leached out of this mass and

were neutralized with acetic acid. The equivalent of 100 gm. of green plant was reserved and the remainder, equivalent to 1400 gm. of green plant, or twice the lethal dose, was administered per os to sheep No. 650. It did not affect the animal. Evidently there is not enough potassium in the plant, *per se*, to account for the range poisoning, and the conclusion is forced that the observed poisoning is due to the mixed salts. From toxicological considerations it is probable that the sodium is relatively harmless and that the potassium and the oxalic acid are the real toxic agents in the plant.

Examination of the Urine of Sheep Fed on *Sarcobatus*.

A number of sheep were penned up singly and were given as much freshly collected greasewood as they would eat, this work forming a portion of Mr. Clawson's experiments. Two of these animals, Nos. 613 and 614, after they had been feeding for some time upon the plant, were put into a metabolism cage and the urine voided during 24 hours was collected. At the time of collection sheep No. 613 had eaten 142.5 pounds in 32 days and sheep No. 614 had eaten 134.75 pounds in 33 days. The results of the clinical examination of the fresh urine follow. An analysis of a 24-hour sample from sheep 613 taken more than two months later, when the animal was wholly normal, is added for the sake of a comparison.

TABLE 2—ANALYSIS OF URINE OF SHEEP.

	Sheep in Normal Condition.	Sheep Feeding on <i>Sarcobatus</i> .	
	No. 613. Sept. 18, 1921.	No. 613. July 12, 1921.	No. 614. July 13, 1921.
Volume	780 ml.	5754 ml.	3495 ml.
Specific Gravity	1.030	1.019	1.023
Reaction	Alkaline.	Alkaline.	Alkaline.
Reducing Substances ...	0	0	0
Albumens	0	0	0
Urea	35.98 gm.	67.21 gm.	43.61 gm.
Total Solids	54.52 gm.	175.79 gm.
Biliary Acids	0	Present.	Present.

Tests for oxalates showed that there was only a very small quantity of combined oxalic acid excreted in the urine.

The Search for Other Toxic Compounds in the Plant. In order to make sure that the oxalates were the only poisonous substances

present in *Sarcobatus* a series of experiments were conducted with fractionated extracts from the plant, and a brief description of this part of the investigation follows.

Volatile Substances. Eighteen hundred grams of the fresh plant was made alkaline by soaking in a solution of 36 gm. of KOH in 5 liters of water and then the mass was distilled. The first portions of the distillate were alkaline, but shortly neutral distillate came over. The distillation was continued until pure water was collected. A quantity of the distillate equivalent to 700 gm. of the plant was administered per os to sheep No. 625, and did not affect the animal.

Saponins. The green plant has a "soapy feel" and its aqueous extracts form persistent froths. Accordingly two different methods for the extraction of saponins were applied to samples of the plant, and the solutions so obtained, which should have contained all of the saponins, if any, present in the plant, were administered to sheep. In no case was any animal affected. In addition, at none of the autopsies of animals which died after being poisoned with this plant was there any evidence of hemolysis.

Portions of the water extract were dissolved in 0.85 per cent. sodium chloride solution and were made up to the following concentrations, calculated to green plant: 4 per cent., 8 per cent., 20 per cent. and 40 per cent. These were tested against a 3 per cent. suspension of washed sheep's corpuscles in normal salt solution, but in no case showed any evidence of hemolysis.

It may therefore be said that toxic saponins are absent from the *Sarcobatus*.

Hydrocyanic acid and cyanides. Routine tests for cyanogen compounds were applied to several of the extracts. None of the tests were positive.

Alkaloids. A portion of the water extracts of the green plant, which, after acidifying with hydrochloric acid, yielded a precipitate with Mayer's solution, was made alkaline with a slight excess of sodium hydroxide and was shaken out with chloroform. On separating the chloroform layer, washing it with faintly alkaline water, and then shaking it with dilute acid, no alkaloid was obtained. The extract was then extracted again by shaking with ether, the ether

layer was separated and treated in the same way as the chloroform solution, and no alkaloid was obtained. It was therefore concluded that the precipitate with Mayer's solution was due to some non-alkaloidal constituent of the plant.

Glucosides. The fact that the water extract of the green plant reduces alkaline copper solutions only after hydrolysis pointed to the probable presence of a glucoside or some disaccharose or polysaccharose. An attempt was therefore made to isolate a glucoside, but without success. The reducing substance is soluble in alcohol and several fractions which contained it were administered per os to sheep. None of these experimental animals were affected by the extracts, and consequently no toxic glucoside is present.

Summary.

The common greasewood of the mountain States (*Sarcobatus vermiculatus*) has been investigated for toxic constituents. Large quantities of potassium and sodium oxalates were found, and these are responsible for the cases of range poisoning. Toxic alkaloids, glucosides, and saponins are absent. Hydrocyanic acid or its compounds was not found in the plant.

The writer wishes to express his thanks to Dr. C. D. Marsh, Mr. A. B. Clawson and Mr. G. C. Roe for their kindly advice, criticism, and assistance during this investigation.

Washington, D. C.

THE VOLUMETRIC DETERMINATION OF PHOSPHORIC ACID AND OF SODIUM PHOSPHATE AND PYROPHOSPHATES.*

By Frank X. Moerk.

The paper on "Methyl-orange as an Indicator in Presence of Indigo-carmin," read at the meeting of this Association in 1921, was followed by another paper read before the Scientific Section of the American Pharmaceutical Association on "Modified Methyl-orange Indicator in Titrating Phosphoric Acid and Phosphates."

*Presented to the 1922 Meeting of the Pennsylvania Pharmaceutical Association.

The important points in these papers are as follows:

(1) The indicator used for quantitative experiments contained 0.1 gm. methyl-orange and 0.3 gm. indigo-carmin in 100 cc. water; as it was found that this mixed indicator deteriorated on keeping, the two reagents were kept in separate solutions and 0.2 cc. of each added to 100 cc. of water, or other liquid, in which the titration was to be made.

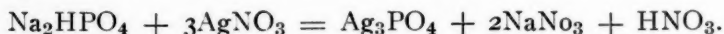
(2) Alkaline hydroxides cause the decomposition of the indigo-carmin and the reaction then is due to the methyl-orange only; if NaOH or KOH is to be titrated it will be necessary to add the NaOH or KOH to an excess of an acid and determine the excess of the acid with an alkali.

In titrating phosphoric acid in presence of excess of calcium chloride or of lead nitrate the indigo-carmin is precipitated and the end-reaction is due the methyl-orange only.

In titrating phosphoric acid in presence of silver nitrate the indigo-carmin is quickly oxidized and the methyl-orange more slowly changed in some way so that a colorless supernatant liquid finally results.

(3) The addition of sodium chloride to solutions to be titrated has the effect of decreasing the amount of acid V. S. in titrating sodium phosphate and of increasing the amount of alkali V. S. in titrating phosphoric acid. The results of adding varying quantities of sodium chloride gave warrant for the concluding statement, "it seems likely that, with the aid of the modified indicator and in presence of sodium chloride, a method will be found for directly titrating phosphoric acid and sodium phosphate; the necessary quantity of sodium chloride will be found to differ for these two substances."

(4) In the U. S. P. IX process for the assay of phosphoric acid and sodium phosphate (the former in a preliminary step is practically converted into sodium phosphate), silver nitrate is added in excess to enable the formation of normal silver phosphate, which, however, is not completely precipitated until a neutralizing agent is added to take care of the acid liberated in the formation of silver phosphate:



For this purpose zinc oxide free from chloride is to be added until a neutral reaction to litmus results; as soluble zinc salts of the mineral acids have an acid reaction to litmus an unnecessarily large excess of zinc oxide may be added. The mixture of liquid, silver phosphate and excess of zinc oxide is next made up to a definite volume, filtered and, in an aliquot portion of the filtrate, the excess of silver nitrate determined and calculation made to phosphoric acid or sodium phosphate; as no allowance is made for the volume of the insoluble material the results calculated from the titration must be low; all salts and acids forming silver salts insoluble in neutral solution will be included in this assay and the results will be correspondingly high.

If a solution of phosphoric acid or of sodium phosphate be mixed with an excess of silver nitrate and then sodium hydroxide V. S. be added from a burette a transient brown color or precipitate of silver oxide will be produced, which disappears quickly upon stirring because changed into yellow silver phosphate; a permanent brown tint shows the end of the formation of silver phosphate and is best seen in a portion of the decanted supernatant liquid. This modification of the silver nitrate process depends upon neutralization and can only be affected by presence of other substances capable of neutralizing alkalies. The working details of this titration will be given a little further on.

Three molecules of silver nitrate will react with one molecule of either phosphoric acid or sodium phosphate, requiring for neutralization, however, with the former three molecules of sodium hydroxide, with the latter one molecule of sodium hydroxide.

Phosphoric Acid.

NaOH V. S. contains in 1 cc. 0.2463 gm. NaOH the equivalent of

0.0603653 gm. H_3PO_4 using indicator;
 0.0201218 gm. H_3PO_4 in presence of $AgNO_3$.

Method of Neutralization Using Indicator.

To 100 cc. distilled water or other specified liquid, add 0.2 cc. each of the methyl-orange solution (0.1 gm. per 100 cc.) and indigo-carmin solution (0.3 gm. per 100 cc.), then add a dilute HCl solu-

tion (about decinormal), drop by drop, until the green color changes without producing a violet color and divide the solution into two equal portions placing these portions in beakers of the same internal diameter. (This procedure will ensure the same tint in both portions, whereas the directions previously given, namely, to add 0.1 cc. of each of the colored liquids to two portions of 50 cc. water, or other specified liquid, and treating these separately with HCl, often gave differently tinted solutions.) To one of these portions add the solution to be tested and titrate with NaOH V. S. until the color matches the reserved portion; for final decision in the matching hold the beakers over a white surface and look down through the liquids. If desired a check titration can next be made by adding another portion of the solution to be tested to the reserved portion and matching this against the previously titrated solution.

Interpret the per cent. NaCl specified in some titrations as grams per 100 cc.

Method of Neutralization in Presence of Silver Nitrate.

Place a calculated excess of 10 per cent. silver nitrate solution which must be neutral (ensured by adding NaOH V. S. to the stock solution of silver nitrate until a brown precipitate forms, allowing the precipitate to settle and decanting the clear solution) in a beaker, add the solution to be tested and then NaOH V. S. with constant stirring; as the yellow silver phosphate becomes bulkier it will promptly settle so that part of the supernatant liquid can be decanted into another beaker and the titration continued; as the precipitate in this beaker increases, the mixture is transferred back to the original beaker, thoroughly stirred, the liquid decanted and titration continued until finally one drop NaOH V. S. produces a brown coloration not changing to yellow upon mixing with more of the supernatant liquid from the original beaker. (The silver nitrate necessary can be calculated from the weight taken for assay or from the results of the neutralization method with indicator; one molecule of phosphoric acid or sodium phosphate or of NaOH or HCl requires three molecules of silver nitrate.)

Results.

Ten cc. H_3PO_4 solution used for each titration:

H_3PO_4 in 10 cc.	A. 1.23431 Gm.		B. 1.08733 Gm.		C. 1.06945 Gm.	
	cc. NaOH	% H_3PO_4	cc. NaOH	% H_3PO_4	cc. NaOH	% H_3PO_4
Water	17.35	84.85	15.25	84.66	15.05	84.95
2.5% NaCl	17.5	85.58	15.35	85.22
5.0% NaCl	17.6	86.07	15.4	85.49
7.5% NaCl	17.7	86.56	15.6	86.61	15.35	86.64
10.0% NaCl	17.8	87.05	15.7	87.16
120 cc. 10% Ag NO_3 ..	53.1	86.56
100 cc. 10% Ag NO_3	46.8	86.61	46.1	86.74

Notice that under the conditions of these experiments using about half-normal NaOH and about one gram H_3PO_4 excellent results were obtained with a 7.5 per cent. NaCl solution.

Sodium Phosphate.

HCl V. S. contains in 1 cc. 0.016277 gm. HCl the equivalent of 0.0633986 gm. Na_2HPO_4 using indicator.

NaOH V. S. contains in 1 cc. 0.02463 gm. NaOH the equivalent of 0.0874454 gm. Na_2HPO_4 using indicator or in presence of silver nitrate.

Method of Neutralization Using Indicator.

Directions as under Phosphoric Acid but titrate with HCl V. S. instead of NaOH V. S.

Method of Neutralization in Presence of Silver Nitrate.

Directions as under Phosphoric Acid.

Results.

Ten cc. of solution used containing 1.0238 gm. anhydrous Na_2HPO_4 :

Water	16.10 cc. HCl	99.70% Na_2HPO_4
2.5% NaCl	16.00 cc. HCl	99.08% Na_2HPO_4
5.0% NaCl	15.90 cc. HCl	98.46% Na_2HPO_4
7.5% NaCl	15.85 cc. HCl	98.15% Na_2HPO_4
10.0% NaCl	15.80 cc. HCl	97.84% Na_2HPO_4
70 cc. 10% Ag NO_3	11.70 cc. NaOH	99.93% Na_2HPO_4

At least two, in many cases three and four, titrations were made without variation in results. From experimental work contained in the previous paper titration of sodium phosphate with an acid V. S. in the absence of NaCl gave in most cases results a little higher than with alkali V. S. in presence of silver nitrate while the titration of phosphoric acid with alkali V. S. in absence of NaCl gave decidedly lower results than with alkali V. S. in presence of silver nitrate. In the above series of titrations the one in which silver nitrate was used gave the highest result; the only change in the working details has been mentioned and consisted in dividing the diluted and neutralized indicator into two equal portions. Another possible explanation suggested itself; in one case the solution was titrated with an acid V. S. while in the process of silver nitrate the solution was titrated with an alkali V. S.; theoretically this indicator should give identical results in the two methods of titrating, but to test the matter there was formulated a

Residual Method for Sodium Phosphate With Indicator.

Proceed with the directions under Method of Neutralization Using Indicator until the solution is divided into two equal portions; then to one portion add a measured quantity of acid V. S. (more than enough to overcome the alkalinity of the sodium phosphate, 20 cc. HCl V. S.), and titrate with NaOH V. S. to match the color of the reserved portion. Then add to the reserved portion the 10 cc. sodium phosphate solution to be used for the test, followed by the same quantity of acid V. S. (20 cc. HCl V. S.) as used in the previously titrated solutions and titrate the excess of acid V. S. with NaOH V. S.; the difference between the two titrations gives the cc. of NaOH V. S. equal to the sodium phosphate.

Results.

Sodium phosphate and volumetric solutions as stated above:

	20 cc. HCl V.S.	For excess HCl V.S.	For Na ₂ HPO ₄	% Na ₂ HPO ₄
Water	14.5 cc.	2.75 cc.	11.75 cc.	100.36
2.5% NaCl	14.5 cc.	2.80 cc.	11.70 cc.	99.93
5.0% NaCl	14.45 cc.	2.85 cc.	11.60 cc.	99.08
7.5% NaCl	14.45 cc.	2.90 cc.	11.55 cc.	98.65
10.0% NaCl	14.45 cc.	2.95 cc.	11.50 cc.	98.22
70 cc. 10% AgNO ₃	11.70 cc.	99.93

Notice that under the conditions of these experiments using half-normal NaOH and about one gram Na_2HPO_4 concordant results were obtained with a 2.5 per cent. NaCl solution.

To ascertain the effect of using a more dilute alkali V. S. in titrating phosphoric acid and sodium phosphate an approximately fifth-normal NaOH V. S. was prepared and standardized with the HCl V. S. (1 cc. 0.016277 gm. HCl). Twenty cc. HCl V. S. were added to the diluted and neutralized indicator and titrated with NaOH V. S.

Water	+	20 cc. HCl V.S. required 42.8 cc. NaOH V.S.
1.0% NaCl	+	20 cc. HCl V.S. required 42.75 cc. NaOH V.S.
2.5% NaCl	+	20 cc. HCl V.S. required 42.75 cc. NaOH V.S.
10.0% NaCl	+	20 cc. HCl V.S. required 42.75 cc. NaOH V.S.

1 cc. NaOH V. S. in absence of added NaCl, or in presence of AgNO_3 represents

0.0083443 gm. NaOH equivalent to

0.0068169 gm. H_3PO_4 in presence of AgNO_3 ;

in presence of 1 per cent. to 10 per cent. NaCl represents

0.00835403 gm. NaOH equivalent to

0.02047489 gm. H_3PO_4 .

Phosphoric Acid.

10 cc. containing 1.06945 gm. H_3PO_4 (86.74 per cent.) in presence of

7.5 per cent. NaCl required 44.9 cc. NaOH V. S. equal to 85.96 per cent.

10 per cent. NaCl required 45.2 cc. NaOH V. S. equal to 86.53 per cent.

In these titrations the final volume of liquid is practically 105 cc. against 75 cc. when the stronger V. S. was used, therefore the NaCl is considerably reduced which as stated before has a marked influence upon the results; by using a 10 per cent. NaCl instead of 7.5 per cent. the percentage of H_3PO_4 is raised to nearly the true content (86.74 per cent.).

Sodium Phosphate.

1 cc. HCl V. S. contains 0.016277 gm. HCl the equivalent of
0.0633986 gm. Na_2HPO_4 in absence of added NaCl;

1 cc. NaOH V. S. contains 0.0083443 gm. NaOH the equivalent
of
0.0296252 gm. Na_2HPO_4 in absence of added NaCl or in
presence of AgNO_3 ;

1 cc. NaOH V. S. contains 0.00835403 gm. NaOH the equivalent of
0.02966 gm. Na_2HPO_4 in presence of added NaCl.

10 cc. solution containing 1.0363 gm. Na_2HPO_4 were added to
the prepared diluted indicator solution and titrated with HCl V. S.,
then the quantity of HCl V. S. was increased to 20 cc. and this
solution titrated with NaOH V. S.

		Direct	Residual		
			cc. NaOH required for		
			20 cc.	Excess	
		HCl V.S. Na_2HPO_4	HCl V.S.	HCl V.S.	Na_2HP_4
Water 16.3 cc.	99.72%	42.8	7.9	34.9 = 99.77%
1.0% NaCl	. 16.25 cc.	99.41%	42.75	8.05	34.7 = 99.31%
2.5% NaCl	. 16.2 cc.	99.11%	42.75	8.15	34.6 = 99.03%
5.0% NaCl	. 16.1 cc.	98.49%	42.75	8.3	34.45 = 98.60%
35 cc. 10% AgNO_3					34.8 = 99.48%

These experiments indicate that with a more dilute V. S., the
NaCl content has to be decreased to check up with the silver nitrate
and NaOH V. S. method.

There is no doubt, from the experiments recorded, processes
can be devised for the assay of Phosphoric Acid and of Sodium
Phosphate, if the weight of a substance taken for analysis, the
strength of the volumetric solution to be employed and the liquid for
the dilution of the indicator are specified.

Experience with the silver nitrate and NaOH V. S. method
impresses one very favorably and so far as I know, is not affected
by variation in the several influences mentioned in the indicator
method. This method will be found suitable for phosphoric acid,
for mono-sodium and for di-sodium phosphate; tri-sodium phos-
phate will give a neutral filtrate after the addition of silver nitrate
and therefore this method will not be applicable.

Sodium Pyrophosphate.

In one of the earlier experiments in which sodium phosphate was rendered anhydrous by heating over a small flame, the supposedly anhydrous phosphate, after weighing, was dissolved in the prepared indicator and titrated with HCl V. S.; calculation made to Na_2HPO_4 gave close to 105 per cent. Some of the same lot of phosphate dried at 110° to 115° C. and titrated in the same manner gave 100.42 per cent Na_2HPO_4 . The high results were explained upon the assumption that the phosphate was at least in part converted into pyrophosphate and that the latter acted towards acid V. S. like the phosphate, in other words, that two of the sodium atoms in the formula $\text{Na}_4\text{P}_2\text{O}_7$ were capable of neutralizing acid V. S.; expressed differently $\text{H}_4\text{P}_2\text{O}_7$ towards the indicator reacts like a di-basic acid.

Many of the text books, including the U. S. P., state that crystallized sodium phosphate becomes anhydrous at 100° C. and at a red heat is converted into pyrophosphate. The lowest temperature at which phosphate becomes pyrophosphate, that I have seen published is 200° C., although the same book in another place gives 250° C.

0.7812 gm. of a sample of crystallized sodium pyrophosphate dissolved in a water dilution of the indicator required 10.1 cc. HCl V. S. for neutralization, which calculated to $\text{Na}_4\text{P}_2\text{O}_7 \cdot 10\text{H}_2\text{O}$ gave 100.06 per cent.

Upon closer inspection, the sample showed some opaque particles; dried at 110° to 115° C., a loss of 39.63 per cent. was noted compared with the theoretical loss of 40.37 per cent. A solution was next made, containing in 10 cc. 0.31294 gm. of the anhydrous salt, and with this solution a series of tests were made similar to those made with the last Na_2HPO_4 solution, and with the same volumetric solutions.

1 cc. HCl V. S. is the equivalent of 0.0593774 gm. $\text{Na}_4\text{P}_2\text{O}_7$.

1 cc. NaOH V. S. is the equivalent of 0.027746 gm. $\text{Na}_4\text{P}_2\text{O}_7$ in the absence of added NaCl.

1 cc. NaOH V. S. is the equivalent of 0.027778 gm. $\text{Na}_4\text{P}_2\text{O}_7$ in the presence of added NaCl.

	Direct		Residual		
	HCl V.S.	$\text{Na}_4\text{P}_2\text{O}_7$	HCl V.S.	cc. NaOH V.S. required for 20 cc. HCl V.S.	Excess $\text{Na}_4\text{H}_2\text{P}_7$
Water	5.2 cc.	98.66%	42.8	31.55	11.25 = 99.74%
2.5% NaCl	5.15 cc.	97.72%	42.75	31.6	11.15 = 98.97%
5% NaCl ..	5.15 cc.	97.72%	42.75	31.6	11.15 = 98.97%

7 cc. 10 per cent. AgNO_3 with 20 cc. H_2O gave a white precipitate turning pink (arsenate?), the decanted liquid gave no further precipitate with AgNO_3 and required 0.2 cc. NaOH V. S. to produce a brown color.

One of the most interesting points shown in these titrations is the comparatively slight influence of NaCl ; should this also be true with stronger solutions it opens the possibility of determining Na_2HPO_4 after converting it into pyrophosphate.

Chemical Laboratories,
Philadelphia College of Pharmacy and Science,
June, 1922.

METHYL-RED IN THE ASSAY OF PHOSPHORIC ACID AND SODIUM PHOSPHATE.

By Frank X. Moerk and Edward J. Hughes.

While the silver nitrate and alkali V. S. method described in the preceding article gave very good results, the discovery of an indicator suitable for this method was considered worthy of further efforts.

Of a number of indicators tried only two, methyl-red and litmus, gave encouraging results.

Methyl-red Indicator made according to the U. S. P. IX responded as follows using three drops per test with approximately deci-normal volumetric solutions:

10 cc. H_2O a red color turning yellow upon addition of 0.025 cc. KOH V. S.

10 cc. H_2SO_4 V. S. required 10.95 cc. KOH V. S.

10 cc. H_2SO_4 V. S. + 40 cc. AgNO_3 V. S. required 10.95 cc. KOH V. S.

10 cc. of a H_3PO_4 solution and 40 cc. AgNO_3 V. S. required 38.4 cc. KOH V. S.

50 cc. AgNO_3 V. S. a red color turning yellow upon addition of a trace of KOH V. S.; 10 cc. H_2SO_4 V. S. added to this neutralized solution required 10.95 cc. KOH V. S.; lastly, the addition of 10 cc. of the same H_3PO_4 solution required 38.4 cc. KOH V. S.

The titration of 10 cc. H_2SO_4 V. S. using the mixed indicator required 10.95 cc. of the KOH V. S. agreeing exactly with the results obtained above with methyl-red.

Methyl-red does not give a sharp end-reaction in titrating carbonates and cannot be used in titrating phosphoric acid or sodium phosphate in the absence of silver nitrate. In titrating the latter substances it was noticed that the red color became quite faint as the silver phosphate precipitated and in subsequent quantitative determinations only one drop of indicator was added at the beginning of the titration the other drops being added, one at a time, as the color faded.

Experiments having for their object the replacement of silver nitrate by another metallic salt, were unsuccessful; one of these experiments, however, was quite interesting: methyl-red added to a mixture of magnesium sulphate and ammonium chloride produced an orange color and required but little KOH to produce a yellow; 10 cc. of a sodium phosphate solution were next added and the yellow color did not change until MgNH_4PO_4 started to precipitate when a red tint was observed; the disappearance of the red and formation of a permanent yellow required a total of 11.3 cc. KOH V. S.; the same quantity of sodium phosphate in the presence of silver nitrate V. S. required 14.3 cc. KOH V. S. showing that the neutralization was not complete in the presence of magnesium sulphate and ammonium chloride.

Litmus Indicator. The use of litmus paper to record final neutrality in the U. S. P. IX assay of phosphoric acid and sodium phosphate suggested a trial with litmus solution; acids in presence of silver nitrate can be readily titrated with an alkali V. S. providing soluble silver salts only are produced, but should an insoluble silver salt be produced, as in the official process, the litmus color disappears before neutrality is reached.

50 cc. AgNO_3 V. S. (tinted blue with litmus solution were made faintly acid with H_2SO_4 V. S. and the blue tint just restored by the addition of KOH V. S.) were mixed with 10 cc. of sodium phosphate solution and titrated with KOH V. S.; the red color became fainter as the KOH was added and finally a colorless supernatant liquid was produced, which, tested with litmus paper, however, still showed an acid reaction; 14.25 cc. KOH V. S. were required before litmus paper showed a neutral

reaction. The solutions used in this experiment were the same as those used in later determinations; calculated to anhydrous Na_2HPO_4 this assay indicated 93.07% Na_2HPO_4 .

The following data covers the standardization of the volumetric solutions used in a comparison of assay processes:

Sodium Chloride V. S. 6.177 grams of NaCl per liter.

10 cc. NaCl V. S. with 20 cc. AgNO_3 V. S. required, in presence of nitric acid and ferric-ammonium sulphate T. S., 9.3 cc. KCNS V. S.

10 cc. AgNO_3 V. S. required, in presence of nitric acid and ferric-ammonium sulphate T. S., 9.95 cc. KCNS V. S.

20 cc. AgNO_3 V. S. are equal to 19.9 cc. KCNS V. S.

50 cc. AgNO_3 V. S. are equal to 49.75 cc. KCNS V. S.

10 cc. NaCl V. S. are equal to 10.6 cc. KCNS V. S.

1 cc. KCNS V. S. is the equivalent of

0.0032582436 gm. of H_3PO_4 , or

0.0047199012 gm. of Na_2HPO_4 .

Sodium Carbonate V. S. 9.518 grams Na_2CO_3 per liter.

10 cc. Na_2CO_3 V. S. added to 50 cc. of neutralized water-dilution of mixed indicator (see under sodium phosphate) followed by 20 cc. H_2SO_4 V. S. required 4.05 cc. KOH V. S.

10 cc. H_2SO_4 V. S. added to 50 cc. of neutralized water-dilution of mixed indicator required 11.25 cc. KOH V. S.

20 cc. of H_2SO_4 V. S. are equal to 22.5 cc. KOH V. S.

10 cc. of Na_2CO_3 V. S. are equal to 18.45 cc. KOH V. S.

1 cc. of KOH V. S. is the equivalent of

0.0031815891326 gram of H_3PO_4 in presence of AgNO_3 .

0.0095447673978 gram of H_3PO_4 with mixed indicator.

0.0138265777 gram of Na_2HPO_4 in presence of AgNO_3 or with mixed indicator.

Comparison of the Results of Assays.

Sodium Phosphate.—2.117 grams of so-called Dried Sodium Phosphate were dissolved in water to make 100 cc. of solution.

10 cc. were used for each of the following determinations:

U. S. P. IX Method:

(1) 50 cc. of filtrate required 4.35 cc. KCNS V. S.

$49.75 - (4.35 \times 2) = 41.05$ cc. KCNS V. S. = 91.52%
 Na_2HPO_4 .

(2) 50 cc. of filtrate required 4.3 cc. KCNS V. S.

$49.75 - (4.3 \times 2) = 41.15$ cc. KCNS V. S. = 91.74%
 Na_2HPO_4 .

Silver Nitrate and Alkali V. S. Method, Methyl-red Indicator.

To 50 cc. of AgNO_3 V. S. add one drop of methyl-red and a trace of KOH V. S. to produce a yellow color, next add 10 cc. of the solution to be assayed and titrate with KOH V. S. until the red or pink color changes to yellow; in the course of neutralization the pink color fades and if a drop of methyl-red restores the red color more KOH will be needed. Three drops of the indicator, using one drop at a time, were found sufficient in the titrations; the silver phosphate, towards the end settles promptly and the comparatively clear supernatant liquid can be decanted, titrated, returned to the original beaker and mixed with the residual liquid and precipitate; after the precipitate settles the operations just described can be repeated as often as necessary until a supernatant yellow liquid is obtained.

Duplicate assays gave 14.3 cc. of KOH V. S. = 93.39%
 Na_2HPO_4 .

Residual Method with Mixed Indicator.

Preparation of the neutralized water-dilution of the mixed indicator. To 100 cc. of distilled water add 0.2 cc. each of the methyl-orange solution (0.1 gm. per 100 cc.) and indigo-carmin solution (0.3 gm. per 100 cc.), then add carefully a deci-normal acid V. S. until the green color changes without producing a violet color (should the latter color be obtained add sufficient alkali V. S. to restore the green color and then more cautiously add the acid V. S.); divide the solution into two equal portions, placing these portions in beakers of the same internal diameter. To one of these portions add 10 cc. of the sodium phosphate solution and 20 cc. H_2SO_4 V. S. and titrate with KOH V. S. until the color matches exactly the color of the reserved por-

tion; in this matching hold the beakers over a white surface and look down through the liquids.

In duplicate titrations 14.3 cc. KOH V. S. were required
= 93.39% Na_2HPO_4 .

Phosphoric Acid.—1.4798 gm. of phosphoric acid diluted with water to make 100 cc. of solution.

10 cc. were used for each of the following determinations:

U. S. P. IX Method (with one change, namely, rejecting the first portion of the filtrate).

50 cc. filtrate required 5.55 cc. KCNS V. S.

49.75 — $(5.55 \times 2) = 38.65$ cc. KCNS V. S. = 85.10%
 H_3PO_4 .

Silver Nitrate and Alkali V. S. Method, Methyl-red Indicator.

Proceed as stated under sodium phosphate.

Duplicate assays gave 40.25 cc. KOH V. S. = 86.54%
 H_3PO_4 .

Neutralization Method with Mixed Indicator.

Use 100 cc. of 10% NaCl solution* instead of 100 cc. of distilled water and prepare neutralized dilution of mixed indicator as given under sodium phosphate. Divide into two equal portions. To one of these portions add 10 cc. of the phosphoric acid solution and titrate with KOH V. S. until the color matches that of the reserved portion.

In duplicate titrations 13.4 cc. KOH V. S. were required
= 86.43% H_3PO_4 .

Comments.

Of the three methods described the U. S. P. IX method is the most tedious one and is bound to give low results for reasons stated in the first article; of the other two methods the one using methyl-red will give the best results working with unknown samples and unknown quantities; the mixed indicator method gives the quickest results but is influenced by the weight taken, the strength of the NaCl solution, the strength of the volumetric solution and, most seriously, by the deterioration of the indigo-carmin solution (a solution used for the experimental work in June was unfit for use in

*Interpret % NaCl solution as grams per 100 cc.

early September). Using a fresh indigo-carmin solution and paying attention to the other factors mentioned, very satisfactory results are obtainable. From the work described in this and the preceding paper the following tabular arrangement shows the conditions for obtaining the best results with the mixed indicator.

Phosphoric Acid:

Weight taken	NaCl solution*	Volumetric solution
about 1. gm.	7.5%	$\frac{N}{2}$
" 1. "	10. %	$\frac{N}{5}$
" 0.1 "	10. %	$\frac{N}{10}$

Sodium Phosphate Dried. Residual Titration:

Weight taken	NaCl solution*	Volumetric solution
about 1. gm.	2.5%	$\frac{N}{2}$
" 1. "	1. %	$\frac{N}{5}$
" 0.2 "	unnecessary	$\frac{N}{10}$

*Interpret % NaCl solution as grams per 100 cc.

Chemical Laboratories, Philadelphia College of Pharmacy and Science, September, 1922.

ETYMOLOGY AND PHARMACY.*

By Charles H. La Wall, Ph. M.

If, as has been said by an eminent scientist, "Life is a resultant of various opposing and co-ordinating forces," it is equally true that every branch of human study and endeavor which has come down from remote ages is an interesting complex of influences, many of which have long since disappeared and been forgotten.

This is particularly true of pharmacy, which is one of the most ancient of the arts and which, in its present state, may be likened

*Read before the 1922 Meeting of the Pennsylvania Pharmaceutical Association.

to a mighty river which has been formed by the confluence of smaller tributaries and streams, some of whose tiny rivulets have all but dried up and disappeared.

Etymology and pharmacy are not directly connected, it is true, but if the origin and histories of the names of things in one of the subdivisions of pharmacy are traced, however briefly, a wealth of material is opened to view which might be pursued further with profit and interest.

Let us pursue this course with reference to our systems of weights and measures. The word "avoirdupois" is of French origin and comes from the words "avoir," to have, and "pois" weight. The word "Troy" is also of French origin, but in this case the application is less direct. "Troyes" is the name of a French town, which was an important commercial center some centuries ago. This was at a time when coins were so frequently clipped or diminished in weight by the sovereigns who issued them as a substitute for a more direct taxation, that they no longer passed for face value, but had to be weighed. The standards of weight for this purpose, which originated in the French city of Troyes, were so satisfactory and so frequently referred to that they became widely adopted for weighing precious metals and later were made applicable to medicines.

The word "metric" comes from the Greek "metron," to measure.

Now taking up the subdivisions of these three systems and beginning in reverse order of their previous consideration, in the metric system, the word "metre" comes from the same root as "metric," the word "litre" comes from a Greek word "litra," signifying a unit of weight in use in ancient times and sometimes translated "pound."

The word "gram" also comes from an ancient Greek weight, "gramma," in use in early times.

The ounce, which is a unit common to both Troy and avoirdupois, is from the Latin "uncia," a twelfth of a pound or a twelfth of a foot, as the case might be, and is from the same root as the word "inch," which is somewhat further removed in its resemblance.

The drachm is from the Attic (ancient Greek), "drachma," a small silver coin often actually used as a weight.

The word "grain" is from the Latin "granum," a small seed or kernel, and was originally the kernel of wheat, as ancient English statutes reveal.

The pound is from the Latin "pondo," meaning weight. The scruple is also from the Latin, the word "scrupulus" meaning a small stone, and in its original tongue the term was used to denote fractional parts of time, measures of length, area, etc.

The pennyweight is from the English and was actually the weight of the coin called the "penny," as established by one of Britain's former rulers.

Taking now the measures of volume, the gallon is from an old French word, "galon," meaning a large bowl. The pint is of dubious etymology. Apparently it comes from the Spanish "pinta," which is a term derived from the Latin "pictus," meaning marked or painted and probably indicates a marked subdivision of a large vessel.

The word "drop" comes from the Anglo-Saxon "dreopan," from which root we also get the commonly used word "drip."

The minim is from the Latin "minus," literally the smallest.

Of the fourteen commonly used terms outlined in the foregoing brief article we have represented Greece, Italy, France, Spain, Saxony and England and the composite character of our art becomes evident.

ABSTRACTED AND REPRINTED ARTICLES

PHARMACEUTICAL CHEMISTRY.†

By Frank R. Eldred.*

The complexity of the problems of life in health and disease is a serious limiting factor in the progress toward more efficient remedial agents. The important advances in this field have usually resulted from the work of many individuals trained not only in chemistry but also in the various branches of biology and medicine. Chemical studies undertaken with no thought of their bearing upon the treatment of disease often supply the foundations for the development of most valuable medicinal products.

†Reprinted from *Journ. Amer. Chem. Soc.*

*Eldred & Atkinson, Inc., Chemical Advisors and Engineers, New York, N. Y.

In an attempt to inventory our progress in medicinal chemistry we are confronted by a vast number of individual researches which contribute directly or indirectly to our knowledge of disease and its treatment by chemical agencies. Progress is probably more rapid than at any previous time, owing to the widespread interest in the subject and to the application of newly discovered chemical principles; nevertheless if we had some adequate means for co-ordinating the work of the army of clinicians, pharmacologists, biologists, and chemists upon whose researches the health and happiness of the human race are so largely dependent, the rate of progress would be increased many fold. Any lack of co-ordination and co-operation in the attack upon disease constitutes a tragedy many times re-enacted.

An example of the time that may elapse between the synthesis of a new compound and the discovery of its physiological properties is afforded by the anti-oxime of perillaldehyde, which was prepared in the laboratory of a German chemical plant in 1910 and nine years later was made the subject of a Japanese patent on account of its sweetening power, which is said to be from four to eight times as great as that of saccharin.

It is consequently difficult to evaluate the progress in this field during any definite period or to give credit to those whose work may lead to most important discoveries. In the limits of this brief review no attempt has been made to give complete references or credit for progress to which many workers have contributed.

During the last two years there has been the usual flood of new remedies, but comparatively few of these represent real progress while many of them are distinctly inferior to products already available.

In many instances there is a marked tendency to return to older forms of medication, which have in the meantime been largely replaced by newer remedies or "pure principles." Some of the so-called pure principles fail to represent the activity of the crude product from which they are derived, thus disclosing the need for further knowledge of the chemistry of the parent product as well as of the substances that can be prepared from it. This is especially true of the crude vegetable drugs, since in the preparation of "pure" plant principles, physical and chemical changes take place, with the resulting destruction of the original colloidal complexes and accompanying changes in the solubilities of active constituents and their ab-

sorption when administered to animals. John Uri Lloyd was a pioneer in pointing out these facts and has made many valuable observations upon the colloidal nature of plant constituents. His original studies, published in the *Proceedings of the American Pharmaceutical Association*, 1876-1889, are very interesting in the light of recent developments.

Digitalis offers an excellent example of the failure to isolate substances which fully represent the physiological activity of the plant. Probably no drug has a more voluminous literature than *digitalis*, which has been the subject of extensive researches by Schmiedeberg, Kiliani, Cloetta, Kraft and many others. Cloetta¹ now reports the isolation of pure crystalline digitoxin which differs from any of the previously prepared digitoxins, all of which are considered by Cloetta to be impure mixtures. Pomeroy and Heyl² suggest the ready hydrolysis of *digitalis* principles as an explanation of the varying results obtained in the investigation of the drug, and also call attention to the observation of Tschirch that, while acetone removes the entire activity from *digitalis* leaf and its aqueous extracts, the acetone extract does not represent the entire activity of the drug. Extraction of an aqueous extract by chloroform resulted in a loss of more than half of the total activity. Tschirch believes that the activity of *digitalis* is due to the mutual effects of the various glucosides and is not the simple sum of the activity of the individual glucosides. Powdered *digitalis* leaf and a tincture or infusion prepared from it are probably the best forms for the administration of *digitalis*, notwithstanding the years of research which have been devoted to this drug. This is also true of many other vegetable drugs which are imperfectly represented by the constituents that have been isolated or from which no active principle has been separated.

Although there is a vast accumulation of data upon the composition of plants, we know very little about the exact physical condition and chemical composition of the substances as they exist in the plant cell before any changes have taken place. The methods which Osborne and his co-workers³ applied in the investigation of fresh spinach and alfalfa would undoubtedly yield valuable results if employed in the analysis of vegetable drugs.

¹ *J. Chem. Soc.*, 120, 1 (1921), 39.

² *Am. J. Pharm.*, 92 (1920), 394.

³ *J. Biol. Chem.*, 42 (1920), 1; 49 (1921), 63.

Cod-liver oil, always popular with the laity, had for a long time been neglected by the medical profession until it was found to be very rich in vitamin-A. Since this discovery was made its use has been constantly increasing and its properties have been generally ascribed to its vitamin content. It has been shown to have a marked effect upon the calcium metabolism, but this property is probably not due to vitamin-A, since cod-liver oil is much more effective than butter fat in preventing rachitic conditions, even when the latter is added to the diet in sufficient quantities to supply much more than the normal requirement of vitamin-A.⁴ It has also been reported that cod-liver oil retains its anti-rachitic properties after the destruction of vitamin-A by exposure to heat and air. It is probable that the physiological effects of cod-liver oil are due in part to its unsaturated fatty acids and its iodine content. It is interesting to note that the American Relief Administration in Russia is supplying cod-liver oil to many day nurseries and children's homes.

Chaulmoogra oil which has been used for many years in the treatment of leprosy with indifferent success has acquired new interest since the preparation of the ethyl esters and sodium salts of the unsaturated acids has made it possible to administer the remedy intramuscularly. Brilliant results are being obtained and the treatment seems to be specific in leprosy.

The administration of substances by inhalation for their therapeutic effects was suggested by the studies of war gases and in some cases this may prove to be a valuable means of treatment. A rather crude attempt is the proposed treatment of tuberculosis by the inhalation of finely divided calcium carbonate. James Todd⁵ has made interesting experiments on the treatment of infected animals by inhalation of ozonized air, and has followed this, with the co-operation of physicians, by the treatment of human cases of tuberculosis and other germ diseases with ozonized oils.

The physiological effects of benzyl alcohol and its esters were studied by Macht, who found that they had a relaxing effect on smooth muscle. Together with the known benzyl esters, a number of new benzyl compounds having the typical benzyl effect have been utilized with success in the treatment of many conditions where a sedative action on smooth muscle tissue is desired.

⁴ *Ibid.*, 50 (1922), 5.

⁵ "Experiments with Oxygen in Disease," Pittsburgh, Pa., 1921.

The relative toxicity of a number of alcohols has been determined by Macht,⁶ who found an increasing toxicity in the series methyl, ethyl, propyl, butyl, and amyl. The secondary alcohols were less toxic than the corresponding primar alcohols. Kamm⁷ tested the normal alcohols on *Paramecia* and reduced his results as well as those of Macht to the numerical expression $1 : 3 : 3^2 : 3^3 : 3^4$ —, the molar toxicity of any member of the series being three times that of the preceding member.

Pure isopropyl alcohol is now available in such quantities that it can be used, where applicable, as a substitute for ethyl alcohol. Although more poisonous than ethyl alcohol, it is also more active as an antiseptic and it might therefore replace ethyl alcohol where used for its preservative action.

Denatured alcohol is finding wider use in the manufacture of medicinal products and in the interest of economy its use will no doubt be further extended.

The autoxidation of ethyl ether, with the formation of ether peroxide, hydrogen peroxide, aldehyde, and acetic acid, which is described by Clover,⁸ may have an important bearing on its use as an anesthetic. The oxidation is greatly accelerated by light.

A number of dyes, particularly the acridine dyes, find a continually increasing use as antiseptics. Further studies in the acridine series have led to the preparation of 2-ethoxy-6, 9-diaminoacridine, which is said to be superior to the acridine compounds now in use. A number of other dyes have been found to be active germicides. Mercurochrome, dibromo-oxymercury-fluorescein, seems to be a very useful urinary antiseptic and Hirschfelder⁹ has found the mercury compounds of saligenin and of *p*-hydroxy-*m*-nitrophenyl carbinol to be effective as antiseptics. Johnson and Lane¹⁰ have prepared several new derivatives of resorcinol, and have found that the phenol coefficients of the series, *viz.*, resorcinol, ethyl resorcinol, *n*-propyl resorcinol, *n*-butyl resorcinol, increase in the following order 0.3, 1.5, 4.3, 8.0. This observation will be of value in future work on antiseptics. The comparative toxicity of germicides to bacteria of dif-

⁶ *C. A.*, 15 (1921), 122.

⁷ *Science*, 54 (1921), 55.

⁸ *J. Am. Chem. Soc.*, 44 (1922), 1107.

⁹ *Ibid.*, 42 (1920), 2678.

¹⁰ *Ibid.*, 43 (1921), 348.

ferent species, or even different strains, is not constant. The application of this "specificity of disinfectants" to the practical testing and use of germicides was first emphasized by Walters.¹¹ It has been found that even the various chlorine disinfectants differ greatly in their relative toxicity to various organisms. Attention is called to the efficiency of steam-distilled pine oil in killing *B. typhosus* and the high resistance of *M. aureus* and *B. anthracis* to this agent.¹²

Cymene and piperitone, a constituent of certain eucalyptus oils, may serve as sources for the commercial production of thymol, one of the valuable remedies in hookworm infections. Carvacrol has been found to be fully as effective as thymol, and since it can be readily prepared from cymene, it should find extensive use. Chloroform and carbon tetrachloride have also been successfully used in hookworm infection.

Cinchophen continues to increase in popularity and a number of closely related compounds have been placed on the market. Bogert and Abrahamson¹³ suggest that a new thiazole derivative which they have prepared, 2-phenylbenzothiazole-6-carboxylic acid, may, from its analogy to cinchophen, have similar physiological properties.

A number of new barbituric acid derivatives have been prepared and some of them have been placed on the market, but barbital seems to be fully as efficient as any of the newer derivatives. Luminal has been found particularly valuable in epilepsy.

The organic arsenic derivatives are the subject of much important research. Arsphenamine and neoarsphenamine remain as the most valuable remedies in syphilis, although promising results have been attained with some of the newer compounds. Much progress has been made in the methods of manufacturing and testing arsphenamine and neoarsphenamine, and products less toxic than the original imported products are now available. Stieglitz and co-workers¹⁴ have prepared 5,5'-mercuri-bis-3-nitro-4-hydroxyphenylarsonic acid and are continuing the investigation with the object of producing a compound for therapeutic use containing both arsenic and mercury.

Bismuth, administered intramuscularly, in the form of potassium and sodium tartrobismuthate suspended in oil or bismuth and am-

¹¹ *Am. J. Pub. Health*, 7 (1917), 1030.

¹² *U. S. Dept. Agr., Bur. Chem., Bull.* 989 (1921), 11.

¹³ *J. Am. Chem. Soc.*, 44 (1922), 826.

¹⁴ *Ibid.*, 43 (1921), 1185.

monium citrate in aqueous solution, is reported to act as a specific in syphilis.

Extensive researches have been devoted to the cinchona alkaloids. Jacobs and Heidelberger have prepared many new derivatives in the cinchona series with the object of finding compounds that will have a specific action in pneumonia. Through the studies of Bass, the quinine treatment of malaria has become much more effective, but it is not improbable that some new derivative of the cinchona alkaloids will be found which will be even more efficient than quinine. An alkaloidal product from *Lobelia inflata* prepared by a patented process is now on the market. Wieland,¹⁵ who studied the alkaloids of lobelia, isolated two crystalline alkaloids, lobeline and lobelidine. These alkaloids will probably be useful therapeutic agents. Cushy has made the interesting observation that *l*-hyoscine is fifteen to eighteen times as active as *d*-hyoscine as a mydriatic, but that the two forms are identical in their action on the central nervous system and therefore in their production of "twilight sleep."

Karrer¹⁶ and co-workers have prepared a number of new amino alcohols and cholines, some of which have an action on the uterus similar to that of ergot. Shepherd's purse (*Capsella bursa-pastoris*), which was used during the war as a substitute for ergot, has been found to contain choline and acetylcholine; the presence of tyramine is regarded as probable and that of histamine doubtful.

The manufacture of digestive enzymes from animal sources has been carried on chiefly for medicinal preparations but they are now being used in increasing quantities in the food, leather and textile industries.

The use of gland extracts in medicine is rapidly increasing and valuable contributions are being made to our knowledge of the composition of these extracts. Notable among such studies is the work of Kendall on thyroxin, the active substance of the thyroid gland. A concentrated preparation of the internal secretion of the pancreas is said to have been used with remarkable success in cases of diabetes. The active principles of the pituitary have not yet been determined, although much progress has been made by Abel, Dale, Dudley and others. Drummond and Cannan¹⁷ state that tethelin

¹⁵ Ber., 54 (1921), 1784.

¹⁶ J. Chem. Soc., 210, 1 (1921), 228.

¹⁷ C. A., 16 (1922), 1974.

is an impure mixture of lipoids, and that the anterior lobe of the pituitary does not seem to influence growth. Ovarian and placental extracts have been found very useful in disturbances of menstruation and pregnancy.

Vitamins are to be considered from the standpoint of foods, as cod-liver oil and certain yeast preparations are the only useful vitamin-containing products that can be classed as medicines. It is possible that with further knowledge of the functions of vitamins and their separation from plant and animal products, vitamin preparations will become valuable as medicines.

McClendon¹⁸ has suggested that our use of refined table salt is a mistake, and that it might be well to substitute a sterilized sea salt which would supply not only iodine, but also numerous other elements which may be deficient in the diet.

The relation of calcium metabolism to rickets has been the subject of much study. Sunlight has been found to have an effect similar to that of cod-liver oil on rachitic animals. Mason states that calcium chloride is better absorbed than calcium lactate and it is interesting to note that a single dose of cod-liver oil administered with the lactate seemed to increase the absorption of calcium.

Colloidal metals have been used, in many cases with apparent success, in combating various infections. Colloidal antimony is reported as being very efficacious in the treatment of leprosy.

Corresponding to the toxic relations between arsenic and arsenious acids, the ions of selenious and telluric acids have been found to be much more effective in killing bacteria than the ions of selenic and telluric acids. Germanium dioxide has been found to stimulate the formation of red blood-cells.

Viewing the manufacture of medicinal products from an industrial standpoint, small-scale operations are the rule and engineering and factory practice is frequently not up to the standard required for larger operations. Much can be gained by a careful study of the methods employed in other branches of chemical industry where success is dependent upon progress in engineering and upon economical management.

¹⁸ *Science*, 55 (1922), 358.

ADEPS HOMINIS: A RELIC OF PREHISTORIC THERAPY.*†

By Dr. M. A. Von Andel, Gorinchem, Netherlands.

One of your illustrious countrymen, Sir James Mackenzie, whose masterly treatises on practical medicine have contributed so largely to enhance the reputation of English clinical science and art on the Continent, in the preface to his work on "The Future of Medicine," describes our art as evolving slowly out of a past, in which facts and fancies, faiths and beliefs, and many superstitions were strangely commingled. Assuming, as we are entitled to do, that medicine has watched over the cradle of mankind, and that there may even have existed an instinctive embryonic sort of medical knowledge before the appearance of man in his present form, we need not be surprised that an art transmitted from such a past has retained down to our own times, vestiges of that remote antiquity, as, analogously, the rudimentary organs of men and many animals preserve the marks of their primitive ancestors.

Survivals.

It would appear, then, that the origin of such relics of the past reaches back to a period prior to that which the history of medicine covers, since it pertains to a stage in the development of the mental faculties of mankind, when emotions, belief, and science had not yet differentiated, and existed only as amorphous germs in the chaotic mass of primitive conceptions. Therefore, these vestiges present themselves to us as transmissions from the dawn of human intelligence, and accordingly may be of service in the study of the depths and intuitions of the untrained mind of our contemporaries which is on a level with that of primitive man. Such survivals generated from the prevailing beliefs of a rude and barbaric society, have lingered on and permeated the official science of later ages, retaining their vitality and authority until finally discredited by the progress of research and the growth and development of rational opinion. Nevertheless, even when officially condemned and refuted by their former patrons, these superstitions have persisted amongst

*Paper read before the Section of Pharmacy, Third International Congress of the History of Medicine, London, July, 1922.

†Reprinted from *The Pharmaceutical Journal and Pharmacist*.

those classes of the population who are still firmly attached to old-fashioned beliefs and customs, or whose mental faculties are not far enough developed to understand, or to value the rationale and results of scientific research, and who, on this account, are at the mercy of the obscurantist sentiment and practice of their class. We shall find that a great number of medicines, and especially those of an animal nature, owe their reputation to factors that seem worthless to us, but nevertheless regard for these factors has excited a powerful influence in keeping alive faith in such remedies, and in perpetuating the use of them which goes back to the childhood of the race, in an age earlier even than that computed by the German medical historian, Höfler, who explains such superstitions in medicine as survivals of ritual sacrifices.¹ It is the object of this paper to adduce evidence in support of the probability of this doctrine from an example occurring in present-day folk-medicine, although it may not be possible to give a definitive solution of so intricate a problem.

Unguentum Adipis Hominis.

Among the many ointments of animal origin in present-day use in Dutch folk-medicine, one reported to contain human fat still enjoys a certain vogue as an application for dislocations and lameness. It usually goes under the name of "Hangman's Salve," or "Poor Sinner's Fat." As, however, capital punishment was abolished in the Netherlands over seventy years ago, there is very little chance of the confiding customer getting the genuine article. What he is likely to receive is a very little portion of suet in a tiny box, and so to fare no better than the hero in the tale of Heinrich Seidel, who sought in vain for gnat's fat to which thaumaturgic therapeutic properties were ascribed. In former times, however, such a miscarriage of *quid pro quo* in the transaction seldom took place. For, in the eighteenth century, genuine *adeps hominis* was still regularly stocked in the apothecaries' shops. One of my compatriots, describing and denouncing the abuses with which the apothecaries of his time were charged, and, in particular, their tendency to trespass on the territory of medical practice, inveighs against them for selling the most revolting compounds, including ointments containing parts of venomous animals, and even human fat,² but that denunciation was far from being just, because human fat was on the list of "simples" in the official dispensaries of that date.

Cures Ascribed to Human Fat.

It will suffice to specify two cases in which human fat was believed to have miraculous powers. A popular author of the seventeenth century relates that a soldier, who was transfixed by a spear, recovered completely from what else had proved a fatal wound by taking as a vulnerary, a mixture of human fat, blood of a he-goat, and Benedict water in beer,³ and an ointment consisting of human fat, dog's fat, and the marrow of a horse-bone was recommended as a sovereign remedy for cramps. These ointments seem to have been in common use, since Vesalius, giving directions for the boiling of the bones of a corpse in order to prepare a skeleton, includes an injunction that the fat floating on the surface of the water should be carefully collected as the fat is held in high esteem as an excellent ointment for wounds, and to restore the functions of tendons and nerves.⁴

Sources of Supply.

The opportunities of obtaining supplies of human fat were not confined, however, to the boiling of corpses for skeleton-making. It was also obtained from the corpses of healthy, vigorous persons who had come to a violent end, that being a *sine qua non* for the medicinal value of the fat. Cabanes records that in 1572, during the massacre of St. Bartholomew at Lyons, the bodies of the fattest victims were delivered to the apothecaries, who extracted the fat from them,⁵ and a similar incident occurred in the history of my native town, Gorinchem, in South Holland. About the date of the massacre of St. Bartholomew the insurgents, or water-beggars as they called themselves, having raided the town, which up to that time had been loyal to the King of Spain, captured about twenty monks, and carried them off to Brielle, where the prisoners were tortured and put to death. The mob treated the corpses of the victims in the most hideous manner. The bodies were cut open, hung on ladders, like the carcasses of pigs, and the fat collected and afterwards sold at Gorinchem presumably because that was the place of origin of the commodity.⁶ Apart from these special cases, other sources of supply were provided by military operations. In Motley's "History of the United Netherlands," we read that during the siege of Ostende (1601), after each engagement, the Dutch surgeons sallied forth over the stricken field and brought back well-filled bags of human fat,⁷ and Johann Dietz, a surgeon who took part in the battle of Ofen

(1686) tells us in his *Reminiscences* that the bodies of the Turks slain in the battle were flayed, the fat boiled out, collected in big bags, and conveyed to the camp of the conquerer.⁸ Another fairly regular, although not abundant, source of supply was the bodies of executed criminals, the fat of which was the perquisite of the executioner, who sold it to, and even treated patients with it, thus becoming an unwelcome competitor with the apothecaries and the medical practitioners. In his "*History of Pharmacy in Cologne*," Alfred Schmidt states that in 1584 the doctors and surgeons of Eger protested against the leave given to the executioner to melt out the fat of his "subjects."⁹ Another and even more gruesome source of supply was from the slowly-mouldering bodies of criminals exposed on stakes. In that case, as a Dutch author informs us, the simplest method was to place vases under the heads of the bodies. Human fat was the principal ingredient in the famous salve with which the executioner dressed the dislocated limbs of the miserable beings who had been subjected to torture.

The Surgeon-Executioner.

This curious conjunction of surgeon-executioner was by no means uncommon in the Netherlands, and with the connivance of the authorities, the dual function survived until the middle of the eighteenth century.¹⁰ In other countries the repute of the executioner and his marvellous salves seems to have been no less prevalent and persistent. In the memoirs of the French Napoleonic soldier, Sergeant Francois Burgogne, an account is given of an untoward incident in which the executioner and his salve played a disconcerting part. Arriving after a fatiguing march at a small Spanish town, Burgogne and his comrades asked their billet-host, an aged bachelor, to procure them some butter or other fat to prepare their meal. He expressed with regret his inability to do so, but, in his absence the soldiers, in searching through the house, came upon three small boxes containing fat, which they "commandeered," and used with their meagre meal of beans. On the return of their host the soldiers took him to task for his inhospitableness, only to learn to their consternation and horror that they had been swallowing human fat which

their landlord, who was the local executioner, had in stock for ointment-making. Even as late as the end of the eighteenth century, during the French Revolution, the fat of the victims of the guillotine was in demand, and Cabanes states, on the authority of de Balzac, that in his time the aristocrats of Sanson sold little boxes of suet to the applicants for "graisse de supplicie."¹¹

A Suggested Rationale.

From the foregoing examples, it is evident that most store was set on the human fat taken from the bodies of persons who had suffered a violent death, and a similar principle runs through the greater part of folk-medicine, in relation to remedial substances of human origin. Therapeutical powers have been vulgarly ascribed to nearly every part or excretion of the human body, and a poetical German apothecary of the eighteenth century has enumerated twenty-two different remedies derived from this source.

It is impossible, within the limits of this paper, even to attempt to prove that the principle of the magical powers of the substances or products of a young and healthy body underlies and actuates similar beliefs and customs of world-wide range. Two typical examples must suffice. These are not strictly medical, but have an evidential value: (a) The salves with which the witches anointed themselves in preparation for the "Witches' Sabbath," in addition to the narcotic herbs, which induced hallucinations, contained the fat of young children, which was believed to have the property of transferring to the witch the vitality and youthfulness of the child from whom it had been taken. This superstition of bygone times finds a parallel in the belief that the fat exuding from the corpses of saints and martyrs possessed miraculous healing powers—*e. g.*, the miraculous oil produced by the corpse of the Abbess Maria van Volckenisse Oerschot, in North Brabant.¹²

As the latter example shows, even at the present time folk-medicine retains some of the superstitions which formerly had a place in orthodox medicine. These superstitions had their genesis in the crude conceptions by which the awakening mind of primitive mankind tried to explain the phenomena of Nature. One of the first forms in which the religious sense reveals itself is derived from and moulded by the feeling that there exists a mysterious interpenetrat-

ing force, manifesting in multitudinous modes, and in such grand categories as energy, vitality, beauty, and sublimity. This mysterious power, which is regarded as partly physical and partly spiritual, is generally denoted by its Melanesian name of "Mana," as it is in Melanesia that the idea exists in its purest form, but a Dutch anthropologist has suggested for it the alternative name of "Soul Substance."¹³ It is conceived of as being bound to and part of all sorts of objects and creatures, and in order to assimilate the desired properties of these objects and creatures, the devotee of primitive magic strives to bring them into external or internal contact with himself, so that he may acquire the vitality, health, or other virtue of the original. On this theory the apparently arbitrary use of many remedial agents of animal origin may readily be explained and classified.

It would be a formidable undertaking to retrace the lines of such a custom back to their primitive sources, as they have found their way down to the present by devious and obscure channels, since, in his lecture on "Early English Magic and Medicine," our President, Charles Singer, distinguished no less than eight elements which contributed to the medical lore of our Anglo-Saxon ancestors, I despair of discovering the true historical sources of contemporary folk-medicine.

In regard to the explanation of the survival of archaic conceptions and practices in medicine, the subject of this paper is of secondary importance. I agree with the folk-lorist Marett that the custom herein described, which has persisted over such a long period, whatever may be its origin, is likely to conform to a given popular standard of mental development. On this ground alone, customs of this type have a psychological interest, as well as a historical value. It is idle to expect to discover what is at the back of the belief or custom by catechising the believers in it. The mental processes and manifestations of the primitive intelligence present the character more of a collective mental reflex than of a distinct personal expression, and are governed chiefly by the hereditary semi-conscious conceptions and instinctive sensations of the group to which they belong, and these are prepotent over the objective observation and interpreta-

tion of the facts. This state of mind, distinguished by Lévy-Bruhl as *mentalité prélogique*,¹⁵ at present still governs the subjective life and external conduct of a majority of our fellow-citizens. Hence it is that the facts and fancies of folk-medicine deserve to be investigated alike as a form of the palæontology of human culture, and as subjects suitable for the elucidation of the reactions of the primitive and untrained mind to phenomena which modern medical science seeks to rationalize.

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SCIENTIFIC AND TECHNICAL ABSTRACTS

PREPARATION OF ALKALOIDAL MERCURIC IODIDES IN A CRYSTALLINE CONDITION. M. François and L. G. Blanc. *Comptes rend.*, 1922, 175, 169-171.—The amorphous precipitate obtained by adding potassium mercuric iodide to a solution of an alkaloidal salt can be brought into solution by warming it whilst suspended in the mother liquor with a large excess of hydrochloric acid; on then allowing to cool slowly it is usually re-deposited in a crystalline form. In the actual preparation of these crystals, the initial precipitation may be avoided by slowly mixing equal volumes of warm solutions of the alkaloidal salt containing a large amount of hydrochloric acid, and of potassium mercuric iodide, of suitable concentrations. A clear solution will be thus obtained from which the alkaloidal mercuric iodide is deposited in crystals on slowly cooling. In this way the mercuric iodides of caffeine, theobromine, quinine, morphine, codeine, cocaine, strychnine, pilocarpine, and sparteine, and also of quinoline, were prepared. They form brilliant yellow crystals, containing no chlorine and no water of crystallization. They show a tendency, well marked in the case of the caffeine compound, but scarcely perceptible with the less soluble compounds, such as that of quinine, to be decomposed by water into mercuric iodide and the alkaloidal hydriodide.—Through *Chemical News*.

G. F. M.

POTENCY OF COMMERCIAL VITAMINE PREPARATIONS.—E. V. McCollum and Nina Simmonds, of Johns Hopkins University (*Jour. Am. Med. Assn.*, 1922, lxxviii, 1953-1957), have tested six commercial vitamine products for vitamine B. Young rats were used as experimental animals; they were given a restricted basal diet for several weeks, then received the same diet plus a commercial vitamine preparation for an additional period of several weeks. The growth curve of each rat was determined. The rats usually gained in weight but little if at all during the administration of the vitamine preparations. The deduction is made that the commercial preparations did not contain vitamine B in concentrated form. McCollum

and Simmonds recommended that milk and leafy vegetables be used to supplement the deficiencies in the ordinary diet and to insure an adequate supply of vitamins. Salads should be eaten twice daily. A liberal helping of greens and a quart of milk or its equivalent in the form of manufactured dairy products should also be taken daily.—Through *Journ. of Franklin Institute*.

J. S. H.

TOXICITY OF GERMANIUM.—The rare element germanium lies next to arsenic in the periodic system. The relative toxicity of these two elements is therefore a matter of interest. F. S. Hammett, J. H. Muller and J. E. Mowrey, Jr., of the University of Pennsylvania (*Jour. Pharm. and Exp. Therapeutics*, 1922, xix, 337-342), have studied the relative toxicity of germanium dioxide and arsenious oxide when administered subcutaneously to albino rats. Arsenious oxide usually produced fatal results when given in a dose of 8 millegrams per kilogram of body weight; sublethal doses caused sloughing at the point of injection. Germanium dioxide in doses as great as 180 millegrams per kilogram of body weight produced neither death nor any apparent evidences of harmful effect; sloughing did not occur at the point of injection. With respect to toxicity, germanium resembles the tin group rather than the arsenic group of elements.—Through the *Journ. of Franklin Institute*.

J. S. H.

MEDICAL AND PHARMACEUTICAL NOTES

COMMERCIAL ACETYSALICYLIC ACID. M. V. del Rosario and P. Valenzuela. (*Philippine J. Sci.*, 1922, 20, 15-22.)—Eight samples of commercial aspirin of German and American manufacture were found to vary in their crystalline form, color and odor, while the melting points ranged from 127° to 136° C., and the percentages of ash from 0 to 0.059. No sample showed the melting point 135° C. given by the Pharmacopœia Germanica; the British Pharmacopœia accepts 133° C. With the odorless samples, that is, those free from appreciable dissociation, the melting point was 136° C., but this was obtained also with samples having an aromatic odor related to

neither acetic nor salicylic acid. Some of the samples when dissolved in alcohol required more than the theoretical proportion of 0.2 *N* sodium hydroxide for neutralization, and in other cases more of the alkali was saturated if the neutralized solution was rendered alkaline and boiled under a reflux condenser. The percentages of free acetic and salicylic acids varied from 0.011 to 0.026 and from 0.002 to 0.015 respectively. If well washed, aspirin should be free from sulphate and chlorine ions; and if it is crystallized from a solvent other than water, its melting point will approach that of the pharmacopoeias and the tendency to undergo hydrolysis will be minimized.—Through *The Analyst*.

T. H. P.

OXALIC ACID IN FOOD.—In the "Queries and Minor Notes" columns of the *Journal of the American Medical Association*, the following figures are quoted in reply to a correspondent who asked: What foods contain calcium oxalate. Calcium oxalate, says the *Journal*, is the usual form in which oxalic acid appears in the diet. The amount of oxalic acid in different articles of food, in parts per thousand, as determined by Esbach, is:—

Black tea infused five minutes ..	2.060
Cocoa-powder	3.520 to 4.500
Pepper	3.250
Coffee	0.127
Parsley	0.006
Common beans	0.158
Potatoes	0.046
Wheat bread	0.047
Crust	0.130
Buckwheat flour	0.171
Barleymeal	0.039
Maize flour	0.033
Sorrel	2.740 to 3.630
Spinach	1.910 to 3.270
Rhubarb	2.466
Brussels sprouts	0.020
Cauliflower	0.003
Beetroot	0.390
Tomatoes	0.002 to 0.052
Carrots	0.027
Chicory	0.103
Endive	0.017

Lettuce	0.016
Dried figs	0.270
Currants	0.130
Prunes	0.120
Gooseberries	0.070
Plums	0.070
Raspberries	0.062
Oranges	0.030
Lemons	0.030
Cherries	0.025
Strawberries	0.012

—*Journ. Amer Med. Assoc.*, July 22, 1922, 321.

THE ANALYSIS OF THE URINE AS A PART OF THE PHYSICAL EXAMINATION OF THE COLLEGE STUDENT. By G. O. Higley, Ohio Wesleyan University.—This work was begun in 1915 because of the death of a college student from diabetes. Tests are made for sugar and for albumin, and in special cases, for other pathological substances. Each year a considerable number of cases of nephritis are discovered, of which about two-thirds show a previous history of an acute attack of that disease.

When any pathological substance is detected a second and often a third sample of urine is tested, and the student is advised to consult a competent physician and to report his findings to the college physical examiner.—Abstract of paper read at the 1922 Meeting of the American Chemical Society.

LESS THAN DROP WOULD DEPOPULATE WORLD.—Poison so powerful that all the people on earth could be killed by one-millionth of half an ordinary thimble full! Drs. Jaques Bronfenbrenner and M. J. Schlesinger, of Harvard University, have found that the strength of the botulinus toxin, which occurs in spoiled vegetable food, is so great that the average man would die from a dose of 0.0000000000000001 cubic centimeters of it.

As there are 473 cubic centimeters in a pint, only an infinitesimal amount would be required to swamp the immigration authorities in Heaven. One cubic centimeter would be enough to depopulate the whole earth with 999,999 parts left over.

Botulinus poisoning was first known as "sausage" poisoning and was detected after fatalities resulting from eating sausage, meats and fish. Recently, this poisoning has been more common after the eating of decayed vegetable foods. It is caused by the bacillus botulinus and, unlike the toxin of diphtheria or lockjaw, it is deadly poisonous when introduced into the body by way of the mouth.

Contamination of foodstuff producing this poison is not common and should such poisoning be present it is usually readily detected by the putrid odor of the food. If the poisoned food is boiled, it ceases to be harmful, while even when the poison is actually consumed, nature and an antitoxin may protect the individual.—Through *Science Service*.

BLEACHING FOODS WITH SULPHUROUS ACID.—Sulphur dioxide has always been considered effective in bleaching foods, but those manufacturers who use this bleaching agent have had great difficulty in removing all traces of the bleach after its work was done. The Government prescribes that food bleached in this way must contain no trace of sulphur. A process has now been patented which enables the manufacturer to use sulphur fumes for this purpose without encountering any difficulty in their subsequent removal. After the bleaching action is finished, enough hydrogen peroxide is added to remove all traces of sulphur dioxide still left in the food. This process can be applied with good results to the bleaching of cherries, gelatine, fruits, syrups, nuts, potatoes, apples and cereals.—From *The Industrial Digest*.

SOLUTION OF SULPHUR IN A MIXTURE OF CARBON DI SULPHIDE AND CARBON TETRACHLORIDE.—M. Serre, of Bordeaux, in order to reduce the inflammability of such a mixture, has worked out the following formula:

Powdered Stick Sulphur 10 gr. 40
Carbon di Sulphide 60 cc.

When solution is effected add carbon tetrachloride to produce 100 cc. and filter. The finely powdered stick sulphur has seemed to be more soluble than any other form.

If carbon tetrachloride is added to a solution of sulphur in carbon di sulphide, a portion of the sulphur is always thrown out,

whether the solution is saturated or not. In the above formula Serre has found the amount to be 0 gr. 40—hence he adds that amount at the start.—From *Bulletin de la Société de Pharmacie de Bordeaux*, through *Répertoire de Pharmacie*.

W. H. G.

ABNORMAL TOXICITY OF CERTAIN CAFFEINES.—A number of samples of caffeine after examination in the Physiological Laboratory of Pharmacie Centrale, have been refused by that house on account of a toxicity above the average.

The manufacturers of these hypertoxic caffeines, when questioned, declared that they had "modified" their process. Desiring to find the cause of this hypertoxicity, this laboratory endeavored to ascertain what bearing the primary source or mode of extraction might have upon the question. Many substances containing caffeine (coffee, tea, tea-dust, kola nut, guarana) were used and several methods of extraction were employed, special attention being given to those used in the industry. All the caffeines thus prepared presented a normal toxicity of 0.24 Gm. to 0.0 Gm. per kilo of animal.

But all caffeines synthetically produced were found to possess hypertoxicity. This abnormal toxicity was laid on uric acid or purines of the same group. Caffeine and uric acid belong to two groups of purines, the first to the dioxy- the second to the trioxy-group.

The experiments in Pharmacie Centrale laboratory seem to prove that the abnormal toxicity of certain commercial caffeines is due to purine bases related to the uric acid group, the presence of which was, very truly, due to "modified" processes designed to augment the product and yield a substance having the physio-chemical, although not the physiological, properties of true natural caffeine.—From *Répertoire de Pharmacie*.

W. H. G.

URINARY CALCULI CONTAINING SILICON.—Urinary calculi are ordinarily composed of urates, oxalates, phosphates, carbonates of lime. Schlicht, in *Pharmaceutische Zeitung*, states that he has found calculi containing chiefly silicon in the bladder of a sheep.

He attributes this formation to feeding upon plants rich in silicon.

W. H. G.

ACTION OF SACCHARIN UPON THE HUMAN ORGANISM.—Since the appearance of saccharin in 1879, and its widely spread use as a sweetening agent in food products, numerous articles have been published which show great divergence of opinion concerning its innocuous nature.

M. Ed. Bonjean, member of The Superior Council of French Public Hygiene, has made a remarkable study of this substance. The result of M. Bonjean's experiments shows that the divergence observed amongst the scientific authors regarding saccharin is principally due to the *acid* action of *pure* saccharin; if this is neutralized by sodium bicarbonate in the manner in which saccharin is actually sold to the consumer, and future experiments carried on therewith, M. Bonjean thinks these divergences will cease. In combination with sodium, saccharin does not at all prevent fermentation—no more than the action of ptyalin, nor that of pancreatin and pepsin. Tablets of sodium-saccharin possess no bactericidal nor antiseptic properties. Ingenious physiological tests of long duration with men and dogs in all doses practically possible, have produced no derangement of digestion or of health. These experiments confirm once more the inoffensive action of sodium-saccharin upon the organism in general.—From *Gazette des Hôpitaux*, through *Répertoire de Pharmacie*.

W. H. G.

FOOD AND DRUG ADULTERATION IN MASSACHUSETTS.—A copy of the recently issued report of the State Department of Health covering the statistics of food and drug examinations in that State for the year ending November 30, 1920, affords interesting reading to the analyst. The report has been prepared under the supervision of Hermann C. Lythgoe, B. S., Director of the Division of Food and Drugs. Considerable space is devoted to milk, the methods of analysis having been carefully examined. Many analyses were made with a view of studying the value of the protein-fat ratio as an indication of adulteration, but it appears that this datum can only be used with several other factors. The amount of liquor submitted by police authorities was larger than in former years. The period covered by the report includes a portion of the period in which the Volstead Act was operative. As might be expected the greater number of samples were from cities. Out of over 1200 samples, 108 were classified as beer, 47 as cider, 165 as wine, 248 as whiskey, 207 as Jamaica

ginger, leaving 454 not specifically classified, but many of these were determined to be distilled liquors of some sort; the majority contained less than 1 per cent. of alcohol. In comparison with former years the samples of high alcohol content have been much more numerous, and distilled liquors have been more than double in proportion. Heavy alcoholic preparations such as ginger extracts and pure alcohol are now nearly four times the proportion formerly submitted.

An interesting case of an adulterated salad dressing is reported. The user called the attention of the department to it because it had produced a "physiologic action" (which is not specified in the report, but which was probably purgation). The nature of the adulterant was at once suspected; inquiry confirmed the suspicion, for it was found that a white mineral oil was being used instead of an edible oil. The fact led to an examination of many other samples, but only two manufacturers were found to be using the material and these promptly discontinued it and destroyed their old stock. A strike in the packing houses in the State led to a suspicion that adulteration of sausages might be practiced, and analysis confirmed it, many samples containing excessive proportion of flour or starch being found. Prosecutions put an end to the practice. Many soft drinks were found to contain saccharin. Attempts were made to attack the law in this case, but were unsuccessful.

Drug adulteration was not found to be extensive, less than 10 per cent. of the samples examined being found objectionable. Half of these were magnesium citrate. A good deal of the activity of the Division was devoted to controlling the cold-storage laws, and many prosecutions were brought under the acts relating to this subject.

The State Department has undertaken the manufacture of arsphenamin. Considerable improvement in the details of the process, especially in the ampouling, have been introduced with resulting economy in operation. Favorable reports from clinical work have been received. The principal expense is said to be the ampouling, which, it is thought, cannot be reduced below 15 cents per ampoule.

H. L.

BOOK REVIEWS

PROTEINS AND THE THEORY OF COLLOIDAL BEHAVIOR. By Jacques Loeb, Rockefeller Institute of Medical Research. McGraw Hill Co., Inc., New York, publishers.

This volume of two hundred and ninety-two pages is a most important contribution, of interest not only to those who are engaged in work on proteins, but also to students of the chemistry of colloids.

The author, by numerous experiments, shows that proteins are amphoteric electrolytes, which form ionizable salts either with acids or with alkalis, and that the behavior of the proteins in this respect is dependent upon the hydrogen ion concentration. There is for each protein a critical point of hydrogen ion concentration at which the proteins refuse to combine; but above this point, they combine with acids, and below, with alkalis, and, indeed, in stoichiometric ratios.

He discusses the swelling of gelatin, and of other proteins, the osmotic pressure, viscosity and other characteristics of their solutions, and reaches the conclusion that colloidal behavior is due to the phenomenon of aggregation which influences the diffusion of the ions and creates the condition referred to in the modern literature of colloidal chemistry as the "Donnan equilibrium," or the "Donnan effect," which, however, is not peculiar to colloids, but may be produced also when two solutions of crystalloids are separated by a membrane, provided one of the ions cannot diffuse through the same, thus creating potential differences and osmotic forces. Indeed, the book as a whole presents forcefully the conviction of the author that proteins are amenable to the general chemical laws.

While the whole scheme of experimentation recorded in this interesting volume was, no doubt carried out as a method of attack on problems in physiology and in pathology, the book is of great importance also to all who are interested in protein products—hence is of interest to the scientific pharmacist.

J. W. STURMER,
Dean of Science, P. C. P. & S.

THE STORY OF DRUGS, A POPULAR EXPOSITION OF THEIR ORIGIN, PREPARATION AND COMMERCIAL IMPORTANCE. By Henry C. Fuller, of the Institute of Industrial Research. Octavo, 343 pages with 85 illustrations. New York, The Century Co., 1922.

Do you realize how immense, how far-reaching, how romantic the drug business is? Are you fully aware what an important rôle drugs play in the health of the nations? The book before us tells the story in as interesting a manner as a novel. It reaches all the way over the known world from tropical India and its spices, to Turkestan and its wormseed, to South America and its many drugs, to the Blue Ridge Mountains and its roots and herbs, to Australia and its asthma weed and other drugs. Its subjects range from rouge and lip sticks to serums and vitamins, from chaulmoogra oil to Lydia Pinkham's Vegetable Compound, from the manufacture of gelatine capsules to the rôle of alcohol in medicine. The author discusses quite fearlessly some questions vital to the drug trade at this time. The book deals with *materia medica*, about which, we are sorry to say, a most unnecessary haze of ignorance has gathered among the public at large.

That in a book of this kind a few errors must necessarily creep in is perhaps excusable. Permit me to call attention to at least some: Cocaine was discovered by Dr. F. Gaedcke not Gardeke (p. 24). It was Dr. Friedrich Hoffmann, not Hoffman (p. 29) who prepared the celebrated anodyne as an opium substitute. Chile saltpeter does not contain KI (p. 11), but NaIO_3 as the chief iodine salt. Trees known as Peru and Tolu (p. 9). Resin of Canada balsam (p. 9). Balsam of Peru is a fragrant aromatic gum—resin (p. 156). Fluid-extract of opium (p. 35). Fluidextract of vanilla (p. 47). It is to be regretted that belladonna *leaves* are used to prepare a type of fluidextract (pp. 47 to 49) as the fluidextract of belladonna root is the one which is official! We must oppose the statement that completely denatured alcohol can be used for bathing and rubbing (p. 83)! Emperor Frederic II did not issue his celebrated edict in 1233 (p. 21), but in 1224, the same year when the University of Naples was founded. It is not a credit to pharmacy that Fuller uses the chemical nomenclature for alkaloids as quinin, codein, etc. However the alkaloid of coca leaves is written cocaine! We hope that in a new edition these errors will be corrected.

This is the first, and so far the only, book of its kind concerned with the actual facts of the drug trade as it exists today. It is an unusual and fascinating book which will prove useful to many men of many minds. Surely pharmacists and others connected with the drug trade should read and study the work!

OTTO RAUBENHEIMER, Ph. M.

FREE PUBLIC LECTURE COURSE

1922—1923

Philadelphia College of Pharmacy and Science

145 NORTH TENTH STREET

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First Lecture.

Wednesday Evening, October 11, 1922.

CHEMISTRY AS AN AID IN THE DETECTION OF CRIME.

By Prof. Henry Leffmann, A. M., M. D.

Lecturer on Research, Philadelphia College of Pharmacy and Science;
Hon. Professor Organic Chemistry, Wagner Free Institute of Science,
Etc.

Chemical processes were early applied in the detection of poisons, and this branch of the science under the title of "Toxicology" still constitutes a most important department of forensic procedure. Of recent years the problem of food adulteration and forgery have become very complex and frequent, and chemical and chemico-physical methods have been applied with much success as well as in other phases of crime. The lecture will include experiments and illustrations of some of the features of this line of work.

Second Lecture.

Wednesday Evening, October 18, 1922.

CORN AND ITS PRODUCTS.

By Prof. Freeman P. Stroup, Ph. M.

Professor of Chemistry, Philadelphia College of Pharmacy and Science.

To many people "Corn" means only something used for the purpose of fattening hogs; others think of it only in connection with "Corn Muffins" or "Corn Pone." To such, an account of the present utilization of the grain, the cob from which the grain has been "shelled," and the stalk which bore the "ears," is apt to be a revelation.

The lecture will include a bit of history of the plant, its growth and cultivation, and the uses of its various parts industrially and as sources of human and animal food, not forgetting the social features that sometimes accompany the harvesting of the crop.

In connection with the lecture, there will be displayed an extensive collection of specimens representing both natural and artificial products.

Third Lecture. Wednesday Evening, November 15, 1922.

THE STORY OF GLASS.

By Prof. J. W. Sturmer, Pharm. D.

Dean of Science, Philadelphia College of Pharmacy and Science.

An illustrated lecture on the glass industry; its growth from the dark glass-less age, to its present-day complexity and importance.

The glass window—how it has influenced our modes of living, and our various lines of employment.

Various types of glass and of glassware; their special uses in the common activities of life.

How glass is moulded and shaped and cut and ground and tinted and decorated. How to select glassware. How to care for it properly.

The lecture will be illustrated with pictures, slides, and with numerous specimens of interest.

Special attention will be given to the more recent developments, and to the newer uses of the various kinds of glass, both in the scientific laboratory and in the common activities of modern life.

Fourth Lecture. Wednesday Evening, December 6, 1922.

VITAMINES.

By Prof. David Wilbur Horn, Ph. D.

Professor of Physics and Physical Chemistry, Philadelphia College of Pharmacy and Science; Professor of Inorganic Chemistry, Wagner Free Institute of Science.

Historical sketch of the chemistry of diet. The experimental establishment of the Laws of Conservation of Matter and of Energy in diet. The inter-changeability of food factors. The protein mole-

cule and the amino acids. Porteins that suffice for normal life. Historical sketch of deficiency diseases. Catalysts, in general. The purification of foods and its effects. Experimental study of accessory food factors. Funk's mistaken "Vitamine." The general theory of Vitamines arising from Funk's error. The present status of Vitamines.

Fifth Lecture. Wednesday Evening, December 13, 1922.

BACTERIAL PREPARATIONS IN COMMON USE.

By Prof. Louis Gershenfeld, B. Sc.

Professor of Bacteriology, Philadelphia College of Pharmacy and Science.

Yeast, *Bacillus Bulgaricus*, and other bacteria sold as such for industrial and medicinal purposes.

Preparations made with bacteria as a starting point.—Of considerable value in industries and in the treatment and prevention of disease: Vaccines, Therapeutic Sera, Antitoxins, etc.

Detailed description and discussion of the above especially for the layman.

Lantern slides illustrating the organisms, steps in the manufacture of the preparations, and other interesting data.

Sixth Lecture. Wednesday Evening, January 3, 1923.

THE ALUMINUM AGE.

By Prof. Ralph R. Foran, P. D.

Assistant Professor of Technical and Analytical Chemistry, Philadelphia College of Pharmacy and Science.

The story of a metal so rare fifty years ago that it was used to make jewelry. Then it cost \$9.00 a pound. Now it costs less than fifty cents a pound and is used in the manufacture of thousands of things, from spoons to automobiles.

It is one and a half times more plentiful than iron and is rapidly supplanting copper for many purposes. The possibilities for its use are unlimited, leading us to believe that we are coming into an "aluminum age."

Seventh Lecture. Wednesday Evening, January 17, 1923.

THE MAKING OF MEDICINES.

(From the time of the Pharaohs down to the Scientific Age of Today).

By Prof. E. Fullerton Cook, Ph. M.

Professor of Operative Pharmacy and Director of the Pharmaceutical Laboratory, Philadelphia College of Pharmacy and Science.

The story of man's continuous effort through the ages, to relieve suffering and cure disease by means of medicines.

A brief review of the past and an account of the new medicines developed by the research of the Medical, Pharmaceutical, Chemical and Biological laboratories of today.

Eighth Lecture. Wednesday Evening, January 24, 1923.

THE COST OF PATENT MEDICINE.

By Prof. Horatio C. Wood, M. D.

Professor of Materia Medica, Philadelphia College of Pharmacy and Science.

The American people spend \$150,000,000 a year on patent medicine. Does part of this money come out of your pocket? If so, you ought to know what you are getting for it. What are the chances of buying improved health? What does it cost to manufacture patent medicines? Are the statements of the venders of these medicines to be believed? Why do people write testimonials as to their cures?

Ninth Lecture. Wednesday Evening, February 14, 1923.

THE NEW ALLOYS OF IRON AND THEIR USES.

By Prof. Frank X. Moerk, Ph. M.

Director of the Technical Chemistry Courses, Philadelphia College of Pharmacy and Science.

Iron, one of the seven elements known to the Ancients, is, and has been for years, commercially the most important metal. The comparative softness, the tendency to oxidize (rusting) and the tendency to crystallize have led to the production of a number of alloys

in which these objectionable properties have been remedied by the addition usually of very small quantities of other metals. The story of "stainless steel."

Tenth Lecture. Wednesday Evening, February 28, 1923.

ANOTHER DROP OF BLOOD.

By Ivor Griffith, P. D., Ph. M.

Clinical Chemist and Serologist, Stetson Hospital, Philadelphia; Instructor in Pharmacy, Philadelphia College of Pharmacy and Science.

A continuation of a former lecture upon the subject. The newer conceptions of its functions, with particular regard to the part which it plays in conveying and utilizing products of the ductless gland laboratories. How these secretions poured into the blood stream are said to affect personality so profoundly that the genius and dullard, weakling and giant, cavalier and puritan, are so only because of inequalities in gland activities.

Eleventh Lecture. Wednesday Evening, March 14, 1923.

THE ROMANCE OF SPICES.

By Prof. Chas. H. LaWall, Pharm. D., Sc. D.

Chemist to Food Bureau, Pennsylvania Department of Agriculture; Professor of Pharmacy, Philadelphia College of Pharmacy and Science.

Many of the spices in common use today are the same as those employed by the Egyptians of the time of Menes and Cheops. In addition to their condimental and culinary uses, spices have occupied an important place in religious observances.

They were formerly valued more highly than gold or precious stones, and the search for their sources and the struggle for the control of these sources when found, has had a profound influence upon the world history. Constantinople, Venice, New Granada, and New Amsterdam, succeeded Rome as central points of trade control, largely because of the rivalry in the spice trade. America was discovered accidentally in the search for a new route to the spice-laden Orient.

The lecture will briefly review this fascinating period of world history. It will be illustrated with specimens, growing plants, lantern slides and experiments.

Twelfth Lecture.

Wednesday Evening, April 4, 1923.

CATALYSIS AND CATALYSTS.

By Prof. Samuel P. Sadtler, Ph. D., LL. D.

Professor Emeritus of Chemistry, Philadelphia College of Pharmacy
and Science.

Earlier views and present views of the nature and meaning of
Catalytic reactions.

Types of Catalytic reactions and practical applications of the
same. Oxidation, hydrogenation, hydrolysis.

Reactions of Organic Compounds. Part played by ferments
and enzymes.

Broad view of Catalysts, and their nature and function.

Illustrations in Industrial Chemistry.

Thirteenth Lecture.

Wednesday Evening, April 25, 1923.

ANIMAL EATING PLANTS.

By Prof. Heber W. Youngken, Ph. D.

Professor of Biology and Pharmacognosy, Philadelphia College of
Pharmacy and Science.

An exposition of the life habits and distribution of a number
of flesh-eating plants, together with the peculiar adaptation of their
varied structures for the allurements, capture, digestion and assimila-
tion of their prey. This lecture will be illustrated with charts and
living examples of types considered.

Fourteenth Lecture.

Wednesday Evening, May 2, 1923.

EXPLOSIVES AND EXPLOSIONS.

By Prof. Henry Leffmann, A. M., M. D.

Lecturer on Research, Philadelphia College of Pharmacy and Science;
Hon. Professor Organic Chemistry, Wagner Free Institute of Science,
Etc.

The lecture will give a brief account of the methods of ancient
warfare, and then take up the nature and actions of the modern low
and high explosives used in peace and war. Explosions due to dust
and gases will be considered. The lecture will be illustrated by lan-
tern slides and experiments.